THERAPEUSIS OF INTERNAL DISEASES

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EDITED BY

FREDERICK FORCHHEIMER, M.D., Sc. D. (Harv.)
Professor of Medicine, Medical Department, University of Cincinnati
(Ohio-Miami Medical College)

VOLUME I

NEW YORK AND LONDON
D. APPLETON AND COMPANY
1918

Printed in the United States of America

PREFACE

THIS work was undertaken because it seemed that a presentation *in extenso* of the therapeusis of internal diseases might be valuable to all those engaged in the practice of medicine.

I venture to say that the subject of the treatment of internal diseases is fast becoming, if it has not already become, one of the most important subjects we have to deal with, either as practitioners or teachers. The reason for this is obvious. Not very long ago the basis of all therapy was empiricism, and empiricism only. Then followed a period in which metaphysical reasoning replaced empiricism, giving rise to the development of schools, and not infrequently of medical sects, some of which still survive even in this period of scientific enlightenment. It may be added that even now new sects are arising, and possibly will continue to arise as long as human credulity survives.

Following this metaphysical period we meet with a most interesting therapeutical manifestation, that of medical nihilism. That great clinician, Skoda, for instance, believed so little in drugs that he treated all his typhoid fever patients by giving them small doses of a weak solution of alum. But, on the other hand, he was the first to place auscultation and percussion upon a physical basis. For him, then, there was no science of therapeusis, although there was science in percussion and auscultation. The nihilistic tendency still has adherents, although their number is small and constantly growing smaller.

Comparatively recently laboratories began to play a very important rôle. Physiology, pathology, chemistry, microscopy, and physics as applied to medicine were being developed, and theoretical therapeutic problems were being solved by laboratory methods, which, in turn, of themselves have become a fetish.

Moreover, there was more careful and accurate observation of disease. But the most conspicuous and important contribution to our therapeutic knowledge in this connection consisted in the acceptance of physiological effects of drugs and their determination. With this to go upon, medical therapeusis received a great and fruitful impetus. It may be

safely said that this was the beginning of scientific medical therapeusis; for the first time it was possible to come to a therapeutic conclusion which was scientific in a measure: the result of observation plus reasoning.

If we now come to our present day we see a remarkable state of affairs. Not only have the therapeutics of to-day been developed beyond anything that could have been hoped for twenty-five years ago, but vistas are being opened which promise advances hoped for only in some dim future state. And yet, if we reflect, the time had come for great and radical advances in this line. The branches of science already mentioned upon which treatment is based had developed to a degree that seemed incredible, and each advance was eagerly seized upon by those who were prepared and ready to apply this development.

Therapeutics, therefore, is beginning to take a place with the other branches of medicine, in as far as its scientific status is concerned. That therapeutics will ever be a pure science seems, at present, out of the question. But the fact that it is what it has developed to be leads us to believe that it is as yet in its infancy.

The great advances that can be recorded in our period are found in prophylaxis and causal or specific therapy.

In prophylaxis, especially in infectious diseases, results are obtained which a short time ago would have been considered impossible. The greatest enthusiast would have deemed it incredible, for instance, that the day would ever come when Havana would quarantine against Key West in yellow fever. Many other instances could be cited in which modern prophylaxis has prevented the spread of disease and the development of epidemics. Indeed, this is now so common that very little ado is made of it. Much more remarkable, however, is the rendering sanitary large tracts of land which were uninhabitable before, thus giving more and better chances for life and health to more human beings.

As wonderful as this seems, the greatest advance made in therapeusis has been in causal therapy. We are no longer solely guided in the use of drugs by their physiological effects, but demand effects upon pathological states and conditions, in this way coming nearer the cause of things and frequently removing it. The treatment of specific causes by specific methods of treatment is especially notable at the present time. Formerly there were two specifics: mercury and quinia. At present there is a large number in infectious diseases, in the form of vaccination with virus from animals less susceptible than man, by vaccinating with

small numbers of bacteria from virulent cultures, by injecting dead bacilli and bacterial products and sera. Relatively still in their infancy, these modes of treatment have already changed the therapeusis of infectious diseases.

Furthermore, there has taken place a revival in the use of physical measures, which have proven themselves very valuable in the light thrown upon them by modern modes of investigation. I refer here to hydrotherapy, balneology, massage and gymnastics, mechanotherapy, electrotherapy, light therapy, Roentgen ray therapy. Nutrition and dietetics have been put upon a scientific basis, and psychotherapy is being applied in a rational way for definite purposes. One of the recent additions to our knowledge, and one which promises much for therapeusis, is physical chemistry. By adding to this list of subjects toxicology, organotherapy, and climatology we have an enumeration of the means applied to the treatment of disease, except of that due to direct medication. If we except this, which it seemed to me required no especial mention or space, as it is discussed and described throughout the book, we have subjects that have a broad general bearing, so that I have grouped them together under the heading of General Therapy and given the whole of the first volume to their discussion. As far as I know, this was first attempted in the Handbuch der allgemeinen Therapie, edited by H. von Ziemssen in 1883. It would seem to me that the grouping of these subjects is invaluable as forming a foundation upon which the whole of therapeusis may be built up. Not alone is this the case, but they serve to bind the various subjects together. The practical value of this division lies in the fact that the general therapeutic measures are fully described and reference can be made to them.

Having then made one division of the whole subject, we follow the Germans and make a second, that of special therapy, which includes the treatment of all diseases which are classified as belonging to internal medicine. Here it is not only the treatment of a special disease, but also the special treatment of a special patient, which makes the subject one beset with great difficulties as well as of transcendent interest. As a result of the complexity of the subject it will be readily seen that there is no branch of medicine which may not have some bearing on special treatment; this applies to anatomy, physiology, physics, chemistry, pathology, symptomatology, pharmacology, to mention only the most important ones. Moreover, the mutual relations of internal medicine to other departments,

such as surgery and the various specialties, must be considered. In these days of multiplication of specialties internal medicine itself may be overlooked, so that only a part of the condition and not the whole is treated. The fact that a prescription is the last act in a long process of reasoning should always be borne in mind.

The prescription should not be written until everything which bears upon the condition of the patient has been considered. It is necessary to make a diagnosis which must include pathology and pathogenesis, this especially for causal treatment. The symptomatology must be carefully investigated, as, in many instances, the relief of symptoms is all that can be done or all that should be done. The therapeutic measures to be taken should then be determined; if drugs, those that fulfill the indications should be chosen. In every case the individual characteristics of the patient should be studied. When all this has been done, the patient is ready for his prescription.

It is in this spirit that the various subjects comprising the work have been treated by the contributors. Everything that has bearing upon therapy is considered, and, as the subjects differ so much, it will readily be seen that uniformity could not be attained. Under all circumstances the primary object is to illuminate the subject of treatment and to give all that is known or worth knowing, and the work is primarily written for all those who wish to be informed of the details of treatment of disease, even the smallest ones.

Prescriptions are given in the text when found necessary; first, on account of showing how the drug is best administered; secondly, the quantity of drug to be given and at what intervals. The days of formulæ are not over, and all of us, it must be confessed, like to employ a formula which has been recommended by a competent observer. All doses of drugs, as well as all prescriptions, are given in apothecary's weight and in the metric system.

The authors who have honored me by writing were chosen because I considered them thoroughly equipped and best able to write upon the subjects assigned to them. Their names and their reputations are a guarantee of the quality of their work.

I wish to express my especial thanks to Drs. William Wherry and Joseph C. Collins for assistance given in the arrangement of these subjects.

F. Forchheimer.

LIST OF CONTRIBUTORS

Maude E. Abbott, B.A., M.D.

Isaac Arthur Abt, M.D.

William Henry B. Aikins, M.D., C.M., L.R.C.P. (Lond.)

Howard S. Anders, A.M., M.D.

Lewellys F. Barker, M.D., LL.D.

Henry Wald Bettmann, B.L., M.D.

Alexander Dougall Blackader, B.A., M.D., C.M., M.R.C.S. (Eng.)

George Blumer, M.D.

Trigant Burrow, M.D.

Charles M. Byrnes, M.D.

Joseph A. Capps, A.M., M.D.

Louis Casamajor, M.A., M.D.

Warren Coleman, A.M., M.D.

Joseph Collins, M.D.

Thomas Darlington, M.D.

George Dock, M.D., Sc.D.

Alvah Hunt Doty, M.D.

Charles Hunter Dunn, A.B., M.D.

Charles Warren Duval, M.D., M.A.

Henry L. Elsner, M.D.

Martin H. Fischer, M.D.

Frederick Forchheimer, M.D., Sc.D. (Harv.)

William S. Gottheil, M.D.

Charles L. Greene, M.D.

J. P. Crozer Griffith, A.B., M.D., Ph.D.

Julius Grinker, M.D.

John T. Halsey, M.D.

Albion Walter Hewlett, B.S., M.D.

Reid Hunt, A.B., M.D., Ph.D.

Smith Ely Jelliffe, A.M., M.D., Ph.D.

Charles G. Jennings, M.D.

Jacob Kaufmann, M.D.

Edward L. Keyes, Jr., M.D., Ph.D.

Herbert Maxon King, M.D.

Sidney Lange, A.B., M.D.

Isaac Ivan Lemann, M.D.

Edwin A. Locke, M.A., M.D.

William J. M. A. Maloney, M.D., Ch.B., F.R.S. (Edin.)

Charles F. Martin, B.A., M.D.

LIST OF CONTRIBUTORS

Edward Ernest Maxey, M.D.

Alexander McPhedran, M.D.

William Fletcher McPhedran, B.A., M.D.

Frank Sherman Meara, A.B., Ph.D., M.D.

Joseph L. Miller, B.S., M.D.

Albert George Nichols, M.A., M.D., D.Sc.

William Hallock Park, M.D., A.B., LL.D.

Howell T. Pershing, M.S., M.D., LL.D.

Allan Ramsey, B.S., M.D.

Charles Ricksher, M.S., M.D.

David Riesman, M.D.

Robert Dawson Rudolf, M.D. (Edin.) F.R.C.P. (Lond.)

John Ruhräh, M.D.

Sidney I. Schwab, M.D.

Henry Sewall, Ph.D., M.D., Sc.D.

Frederick Cheever Shattuck, A.M., M.D., Sc.D., LL.D.

Burt Russell Shurly, B.S., M.D.

Bertram Welton Sippy, M.D.

William H. Smith, A.B., M.D.

William Benham Snow, M.D.

Louis Starr, M.D., LL.D.

Charles G. Taylor, M.D.

Wilder Tileston, A.B., M.D. (Harv.)

Victor Clarence Vaughan, M.D., Ph.D., Sc.D., LL.D.

Creighton Wellman, M.D.

William Buchanan Wherry, A.B., M.D.

Charles Spencer Williamson, B.S., M.D.

Edward Jenner Wood, S.B., M.D.

Francis Carter Wood, B.S., M.D.

Paul Gerhardt Woolley, B.S., M.D. (J.H.U.)

Edwin G. Zabriskie. M.D.

CONTRIBUTORS TO VOLUME I

WILLIAM HENRY B. AIKINS, M.D., C.M., L.R.C.P. (LOND.)
Consulting Physician, Toronto General Hospital, Toronto Hospital for Incurables, King Edward Sanitarium; Radium Therapeutist, Grace Hospital, Toronto
Radium Therapy

LOUIS CASAMAJOR, M.A., M.D.
Chief of Clinic, New York Neurological Institute; Assistant Attending Neurologist, City Hospital, New York
Psychotherapy

WARREN COLEMAN, A.M., M.D.
Professor of Applied Pharmacology and Clinical Medicine, Cornell University Medical College; Visiting Physician to Bellevue Hospital, New York
Nutrition and Dietetics

MARTIN H. FISCHER, M.D.
Joseph Eichberg Professor of Physiology, University of Cincinnati
Some Physicochemical Principles in Therapy

REID HUNT, A.B., M.D., Ph.D.
Professor of Pharmacology, Hygienic Laboratory, U. S. Public Health Service, Washington, D. C.
Organotherapeutics

SIDNEY LANGE, A.B., M.D.
Lecturer on Radiology, University of Cincinnati, Radiographer to Cincinnati General Hospital
X-Ray Therapy

WILLIAM J. M. A. MALONEY, M.D., Ch.B., F.R.S. (Edin.)
Professor of Nervous Diseases, Fordham University, New York City
Hydrotherapy and Balneology

CHARLES RICKSHER, M.S., M.D.
Formerly Chief of Clinic, New York Neurological Institute
Mechanotherapy

HENRY SEWALL, Ph.D., M.D., Sc.D.
Professor of Medicine, University of Colorado
The Principles of Medical Climatology

WILLIAM BENHAM SNOW, M.D.
Founder of the New York School of Physical Therapeutics
Electrotherapeutics; Radiant Light and Heat Therapy

CHARLES G. TAYLOR, M.D.
Massage and Gymnastics

VICTOR CLARENCE VAUGHAN, M.D., Ph.D., Sc.D., LL.D.
Dean and Professor of Hygiene, Department of Medicine and Surgery, University of Michigan
Toxicology

FRANCIS CARTER WOOD, B.S., M.D.
Director of Cancer Research, Columbia University; Pathologist and Attending Physician to St. Luke's Hospital, New York
Vaccine and Serum Therapy

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THERAPEUSIS OF INTERNAL DISEASES

VOLUME I

I. GENERAL THERAPY

CHAPTER I

SOME PHYSICOCHEMICAL PRINCIPLES IN THERAPY

MARTIN H. FISCHER

It is safe to say that the ultimate test of every teaching in medicine and surgery lies in prognosis and therapy. A correct prognosis means that we understand the course of the diseased process with which we are dealing; it is favorable if we are able to retard, stop, or reverse the series of physical or chemical changes that have placed a patient in the diseased state in which we find him; or unfavorable if we are unable to do this. A successful therapy means that we not only understand this matter of prognosis, but also that we have at our disposal appropriate measures by which we may retard, stop, or reverse the course of the diseased process.

We like to believe, and aim to make, our therapy rational. Through the ages there have come down to us the results of the observations of many men who, seeing that a diseased process was modified, say through the laying on of hands, or through the consumption of sea-weed, have recommended such procedures subsequently to patients similarly afflicted. Such therapy is not rational, but empirical. But just because it is empirical it is not to be despised. A therapeutic procedure that brings good results is never to be despised; it usually merely represents the phenomenon of a practical result that has been attained sooner than the interpretation of the mechanism of this result. So, to return to our illustration, we recognize in the laying on of hands the psychotherapy of to-day, and in the administration of sea-weed the consumption of iodids.

But, while we may not despise any good therapeutic procedure just because it is empirical, we have every reason to despise the modern therapist who employs the empirical method where a rational one is at hand, or who employs the empirical method in the hope of winning thereby new and valuable means of combating disease. Such may result, but the methods employed are uneconomical. So, instead of exhausting a pharmacopeia and the time of a hundred workers in trying to find a curative agent for myxedema, it is better to understand the physiology and the pathological physiology of the thyroid gland, and then the beneficent effects of the administration of thyroid gland can almost be told in advance.

What we have just illustrated by reference to myxedema holds true for all our therapy, whether we would practice, as far as possible, a rational therapy now, or whether we are interested in the advancement of this branch of medicine. We ignore the fact too completely in medicine that a rational therapy can be built only upon a rational pathology, and that a rational pathology is impossible without a knowledge of physiology. Physiology, which is to-day a mere gargoyle, will yet become the keystone of a modern medicine.

When we have realized these simple truths for the good of the development of a scientific therapy, we need next to appreciate the fact that the unit for consideration in physiology, and so in pathology and therapy, is the cell. As we are practical men in medicine, we are likely to lose sight of this fact, or to take exception to it, and yet the most practical man, as we shall see, will heed the physiology of the cell most. The reasons for this are obvious.

When a man falls ill, be the cause what it may, he does not do this "all over." Only individual parts of the body may be affected or some parts of the body are affected sooner or more intensely than others. So a man may be poisoned by an infection, and this poison may kill his heart muscle cells, in consequence of which the rest of his body cells then die, for because the heart has failed no oxygen is now supplied the remaining tissues of the body. Or, through a rapid loss of carbon dioxid from the body, the cells governing respiration in the medulla are no longer excited to activity, and so the respiratory movements cease, the blood is no longer oxygenated, and the rest of the body cells die because they are deprived of oxygen. We could give similar illustrations for the liver, or the kidneys, or the thyroid, or any other organ of the body. It is the injury to certain cells in each case that furnishes the characteristic signs of any pathological entity, and, if this injury or the death of these cells removes a condition upon which the life of cells in other parts of the body depends, then these, too, die. And so the whole body may die. The individual cells of a multicellular organism are like the ordinary ameba, only in the complex organism certain functions (possessed also by the ameba) have been especially developed and predominantly assumed by

groups of these cells. These functions have come to be of particular importance only because they have this character of exercising a function upon the proper execution of which the remaining cells of the complex body are dependent (respiration, circulation).

In a complex organism we may, therefore, distinguish between a *general* physiology (common to all cells) and an *organ* or *special* physiology. When we remember that such organ or special physiology scarcely ever represents more than an unusually prominent development of some function of *general* physiology, the necessity and the predominant importance of the general physiology of the cell become manifest.

These remarks will serve to show why, in our discussion of certain therapeutic principles that are of service in daily practice, we find ourselves beginning with a discussion of the behavior of the individual cell. To be familiar with the effect of various external conditions upon the general behavior of the individual cell is to be familiar with the behavior of these same conditions upon groups of cells; and if such groups of cells (an organ) are part of and determine the behavior of yet other groups of cells in a complex organism, to be familiar with the action of these external conditions upon the individual cell is to be familiar with their action upon the organism as a whole. Hence the importance and our interest in the physicochemical constitution of the individual cell. An understanding of the most specialized therapeutic procedure is almost invariably dependent upon such a knowledge of the cell. So we shall find the behavior of salvarsan to be but a brilliant illustration of the way in which a therapeutic agent distributes itself unequally between two cells (spirochete and body cell); the action of the cathartic salts but the therapeutic expression of the general effects of such salts upon all plant and animal protoplasm; the salt-free diet a procedure to be looked upon with suspicion in practice, because the claims for its good behavior are unsupported in the general physical chemistry of the cell.

THE GENERAL CONSTITUTION OF LIVING MATTER

The living matter of which all cells are composed needs, from a therapeutic standpoint, to be considered from the same viewpoint as its physiology, namely, from a purely physicochemical one. Ultimate principles of therapy must be physicochemical in character (1).

In our special discussion we shall deal but little with the purely chemical aspects of the constitution of living matter. It is enough for us to remember that the various chemical constituents of the living cell are easily grouped under the general headings of the proteins, the carbohydrates, the fats, the salts, and water. But the biological significance of the purely chemical attributes of these classes of compounds seems at the

present time in our scientific progress to stand largely behind that of certain physicochemical characteristics possessed by these same substances, and so we find it convenient to regroup these chemical entities under the headings of *the colloids, the crystalloids, and water.* We will consider these seriatim, for in a correct understanding of their physicochemical behavior are concealed the principles that govern much of our modern therapy.

1. The Colloids

The bulk of living matter is made up of colloidal material (2). It will not surprise us, therefore, to discover that the behavior of colloidal material is identical with much that we consider characteristic of living matter.

It is now more than fifty years since Thomas Graham recognized that different chemical substances differ greatly in the rate with which they diffuse through solvents of various kinds. On the basis of this observation he made a distinction between those which diffuse slowly and those which diffuse very rapidly. As the former are for the most part amorphous, and since ordinary glue is an example of this class, he called them colloids. The group that diffuses readily he called crystalloids (3), for such beautiful crystallin substances as cane sugar, ordinary salt, and urea are found in it.

Since Graham's studies, we have become familiar with further characteristics of colloids and crystalloids. Crystalloids are ordinarily stated to form true solutions. This colloids do not—they form pseudosolutions, that is to say, they simply remain suspended in the solvent. Colloidal solutions are, therefore, not homogeneous, but heterogeneous, in their make-up.

Solutions of crystalloids show an osmotic pressure which is proportional to the number of particles of dissolved substance in the unit volume of the solvent. Upon this fact and the minuteness of the dissolved particles depends the diffusibility of the crystalloids. The most typical colloids, on the other hand, show practically no osmotic pressure, and correspondingly do not diffuse at all.

The enormous differences in osmotic pressure between crystalloids and colloids correspond to similar differences in the molecular weight of the substances composing the two groups. The molecular weight of the most pronouncedly colloidal bodies may be measured in thousands, while two or three hundred covers the weight of crystalloids, even when very complex organic compounds are concerned. The following table taken from Rudolf Höber (4) shows this very well. The figures refer to 10 per cent. solutions of the various substances:

Substance.	Mol. Wt.	Osmotic Pressure in Atmospheres.	Depression of Freezing Point.
Methyl alcohol	32	70.00	5.781
Urea	60	37.34	3.084
Glucose	180	12.43	1.027
Cane sugar	342	6.54	0.540
Albumose	2,400	0.93	0.078
Albumin	13,000	0.17	0.015

Crystalloids can, moreover, diffuse uninterruptedly through colloidal membranes, such as animal bladders, intestines, sheets of agar-agar or gelatin. Colloids are for the most part unable to do this. Upon this fact is based the principle of dialysis, in which crystalloids are separated from colloids by placing the mixture in a tube of parchment or an animal bladder and hanging the whole in water or some other solvent. The crystalloids diffuse out, leaving the colloids behind.

It must be stated, at once, however, that between the two extremes of the typical colloids, and the typical crystalloids, there is found an infinite number of substances which lean more or less strongly toward one side or the other. It is possible, for example, to obtain in a crystallin form certain albumins which may ordinarily be taken to represent our most typical colloids. Egg albumin may be obtained in such a state, and the physiological chemist is rarely satisfied with a hemoglobin that is not beautifully crystallin. On the other hand, comparatively simple bodies, such as silicic or tungstic acid, are found in the group of our most representative colloids. These few facts will suffice to show that no hard and fast line can be drawn between the colloids on the one hand and the crystalloids on the other.

It should be clearly understood that, while we speak of colloids and crystalloids, and therefore are seemingly classifying substances, we ought really to speak only of the colloidal and the crystalloidal *state*. Our familiar use of the terms colloid and crystalloid has grown out of the fact that certain chemical compounds are best known to us in the colloidal state, while others we see almost always in a crystalloidal state. As a matter of fact, it is probably safe to assume that any substance may be obtained in a colloidal form, even those simplest and most typical crystalloids, the chlorids of the various metals. That many typical colloids may, on the other hand, be obtained in crystallin form is evidenced almost daily by the ever-growing list of biological products long known to us only in the form of amorphous powders, mucilages, and syrups which chemists are obtaining in crystalloidal form. These considerations are not without biological significance, for a chemical substance in a colloidal form may, and usually does, possess entirely different properties from

the same chemical substance in a crystalloidal form. This fact has been abundantly proved within the last decade in many striking ways. The question of *how* a crystalloid passes over into the colloidal form, or vice versa—a question which has as yet been scarcely investigated physico-chemically—is, therefore, of the greatest importance to biological chemistry, for these very conversions of colloids into crystalloids, and crystalloids into colloids, are among the commonest phenomena observed in the living organism. The question of glycogen formation from dextrose, for example, represents such a change. Coupled with the chemical change of a dehydration, there is in this case a physical change which converts a freely soluble, osmotically active, diffusible crystalloid into an insoluble (pseudosoluble), osmotically inactive, non-diffusible colloid.

Marked as are these differences between colloids and crystalloids (the colloidal and the crystalloidal state), the colloids themselves do not all possess the same properties. Because of this, various attempts have been made to classify the colloids, but it cannot be said that these classifications have been particularly satisfactory. Not only do colloids differ from each other in very essential qualities, but one and the same colloid may exist in two or even more states. A. A. Noyes (5) distinguishes between those colloids which are viscous, gelatinizing, and not readily coagulated by salts and those which are non-viscous, non-gelatinizing, and readily coagulated by salts. To the former of these groups belongs, for example, a solution of gelatin, albumin, globulin, glue, or dextrin, while in the latter might be mentioned the colloidal solutions of ferric hydroxid, aluminium hydroxid, various metallic sulphids, and hemoglobin. What amounts for our purposes to a very similar classification is that of Perrin (6), who distinguishes between those colloids which in the solid state are rich in water and those which are poor. The former of these Perrin designates as hydrophilic colloids, for the latter the name hydrophobic colloids has been suggested. For the purposes of biology these terms are excellent, and in large part adequate. For the purposes of physical chemistry in general they have the drawback of not being sufficiently broad. Water is not the only solvent that may form the base of a colloidal solution. To meet this objection Herbert Freundlich (7) has proposed the name lyophilic colloids for those which show an intimate relationship to their solvent, while those which do not do this are called lyophobic.

Wolfgang Ostwald (8), who has taken a valuable step forward in the proper classification of the various colloids, distinguishes between the emulsion colloids and the suspension colloids, the former of which represent colloidal solutions formed through mixture of two liquid phases, the latter through mixture of a solid with a liquid phase. A separation of the two phases is difficult to obtain in the emulsion colloids, which correspond, it will be seen, with Noyes's first group and Perrin's hydrophilic colloids, while the ready separation of the phases in Ostwald's sec-

ond group brings to mind Noyes's second group, and the hydrophobic colloids.

When we recall that the hydrophilic colloids which have thus far been accorded most study—gelatin, dextrin, starch, glue, vegetable fibers, albumin, gums—are, for the most part, derived from biological sources, their probable importance to the living animal or plant must at once be suspected. Not only is the chief mass of the living organism built up of colloidal material, but most of it belongs in the hydrophilic group. We shall not be surprised in consequence to find that those physicochemical characteristics which make for the division of all colloids into two great classes will show themselves of importance in determining the biological behavior of the tissues.

2. The Crystalloids

The crystalloids may be divided into two great groups, the *electrolytes* and the *non-electrolytes* (9). We shall find that the characteristics that make such a division possible in the realm of pure physical chemistry also distinguish the biological behavior of these two groups from each other.

Substances which when dissolved in water (and certain other solvents) conduct the electric current are known as *electrolytes;* those which do not do this as *non-electrolytes.* All the acids, bases, and salts (particularly the stronger acids, the stronger bases, and the salts formed by their union) are electrolytes, while the various sugars, urea, ethyl alcohol, glycerin, etc., are familiar non-electrolytes. Pure water (practically) does not conduct electricity. Neither will it do this when such a substance as dextrose or ethyl alcohol is dissolved in it. But the water conducts well as soon as any electrolyte, such as sodium chlorid, is added to it.

The effects of electricity upon the living body, whether for good or ill, are possible only because living matter contains various electrolytes. All therapeutic electrical effects are rendered possible because the body contains electrolytes.

The electrolytes behave as they do when dissolved in water because in this solvent they are electrolytically dissociated. The atoms and groups of atoms that are the product of such a dissociation are electrically charged (herein differing from the ordinary atoms), and are known as *ions.* Thus, absolutely pure nitric acid (containing no water) does not conduct the electric current; nor will it if it is dissolved in some solvent that does not lead to an electrolytic dissociation of the acid. This is because under these circumstances only the molecules (HNO_3) of the acid are present. But let water be added to the nitric acid, and this at once dissociates into its two ions (H^+ and NO_3^-), which carry positive and negative charges of electricity. In an entirely similar way sul-

phuric acid dissociates into the ions H^+ and SO_4^{--}; sodium hydroxid into Na^+ and OH^-; sodium chlorid into Na^+ and Cl^-. The ions which carry a positive electrical charge wander to the cathode, and are known as *cations;* those having a negative charge move in the opposite direction, toward the anode, and are known as *anions.* Thus hydrogen is the cation of hydrochloric acid (and of all acids), while chlorin is the anion of this same acid (and of all chlorids).

The degree to which a substance in solution is dissociated differs with different substances and varies with the same substance under different external conditions. The greatest degree of dissociation is shown by the so-called *strong* acids, bases, and salts, as, for example, hydrochloric, sulphuric, and nitric acids; sodium, potassium, and calcium hydroxids; sodium chlorid, potassium sulphate, calcium nitrate. But dissociation, even for these, is complete only in extremely dilute solutions. The degree of dissociation increases with every rise in temperature.

For the most part there exist always a certain number of undissociated molecules beside the ions which are the products of the dissociation. For the common salts that we find in our bodies, and under the conditions prevailing in the body, it is ordinarily held that about eighty-five per cent. of the salt present is dissociated into ions, while fifteen per cent. remains in the molecular state. This means that, for every one hundred molecules of sodium chlorid, for example, present in the body, fifteen are present as such, while the remainder have dissociated to yield eighty-five sodium ions and eighty-five chlorin ions.

It is clear after what has been said that, in dealing with the behavior of any substance in solution, this matter of electrolytic dissociation becomes of great importance. If we deal with a substance that is incapable of dissociating electrolytically, or with one familiarly known to us as an electrolyte, but existing at the time under conditions which render dissociation impossible, then it follows that all the effects noted must be due to the properties of the molecules present. A non-electrolyte can exhibit only molecular effects. This holds whether we deal with its properties in the form of a simple solution in the chemical laboratory, or with its biological behavior as brought to our notice by using this same substance as a food or drug (saccharose, glycerin, alcohol).

In the case of an electrolyte, on the other hand, we have to consider not alone the effects of the molecules, but in addition the effects of the ions yielded on dissociation, and not the effects of all the ions together, but of the individual kinds of ions. So, the effects of sodium chlorid become those of molecular sodium chlorid, of the ion sodium, and of the ion chlorin. If the degree of dissociation is very small, the ionic effects are correspondingly small; if this is great (complete), then the effects of the electrolyte may be entirely the sum of the effects of the separate ions that are yielded on dissociation.

3. Water

The water found in living matter and in the media surrounding living matter owes its great physiological importance to its solvent properties. The various chemical reactions that are characteristic of and necessary for the maintenance of life are rendered possible by this means, for the solvent properties of water make it possible for the dissolved substances to be brought in contact with each other. Water dissolves not only solids, such as sugar or salt, but liquids, such as alcohol, or gases, such as oxygen or carbon monoxid. The solutions resulting therefrom still possess many of the ordinary physical properties of water, but new ones also appear, which depend upon the quantity and the character of the substance dissolved. But the previous state of the dissolved substance is of no importance; the resulting solution is the same, for example, whether we add to water a certain weight of alcohol in the liquid state or in the gaseous state.

We ordinarily think the water in protoplasm to be like the distilled water contained in a test tube in the laboratory. This is largely true, but not entirely true. The water contained in living matter has the property of dissolving solids, liquids, and gases, as has our ordinary water. But the state in which the water is found in the test tube and in living matter is not entirely the same. The water found in the body exists almost wholly in the form of *hydration water* (10); that is to say, the water forms a compound with protoplasm. This is true not only of the water found in cells, but even of the water found in the blood and in the lymph. Uncombined, "free," water analogous to the distilled water in our laboratory test tube is found only temporarily, and in small quantities, in the living animal. As soon as it appears it is excreted. We shall see how important is this distinction between hydration and free water in the body as we proceed. The maintenance of all secretion depends primarily upon the obtaining of free water, and, as the elimination of all poisonous products from the body, whether formed in the normal metabolism of the body or introduced from without (arsenic poisoning), or manufactured in the body in consequence of the introduction of a pathogenic organism into it, is secondary to such a secretion of water, we shall see how important these physicochemical facts are from a therapeutic standpoint.

STANDARD SOLUTIONS AND COMPARATIVE METHODS IN PHARMACOLOGY

Owing to the fact that many of the chemical materials used in therapeutics represent mixtures of many substances (as, for example, the various extracts, fluid extracts, and tinctures prepared from plants), ac-

curate quantitative studies on pharmacological behavior have in large part been difficult or impossible. Quantitative methods have increased hand in hand with advances in chemistry that have given us, in place of mixtures, the well-defined chemical bodies that we know as the alkaloids and the chemically constant active principles of various plants and organs. Yet, in the comparative study of the behavior of such well-defined chemical compounds, to which we can at once add the various acids, alkalies, and salts that form a goodly portion of our therapeutic armamentarium, we have gotten only little beyond the point in which *percentage solutions* of the various compounds are used. In order to make proper comparisons between the pharmacological action of various chemical compounds, it is necessary for us to compare amounts that are not simply equivalent in weight (as in percentage solutions), but that are equivalent from various physicochemical points of view. A definition of a few standards used in this regard is, therefore, in order, for we shall have to use these in our further discussion. Comparative studies with solutions of equal percentage are practically worthless, for reasons that will appear shortly.

The *gram-molecule* is a convenient unit. This is the molecular weight of the substance under consideration expressed in grams. A gram-molecule of hydrochloric acid is 35.46 grams; of sodium chlorid, 58.50 grams; of ethyl alcohol, 46.05 grams. If the substance contains water of crystallization the molecular weight of this expressed in grams is added to that of the substance itself. A gram-molecule of dried sodium carbonate (Na_2CO_3) is 106.10 grams, but of the crystalline compound (Na_2CO_3 $10\ H_2O$) it is 286.26 grams.

A *gram-molecular solution* (or a *molecular* or *molar* solution) contains a gram-molecule of any substance dissolved in enough water to make a liter. If only one-half the gram-molecular weight is dissolved in enough water to make a liter we have a one-half molecular solution; if one-eighth the gram-molecular solution is present in the liter, a one-eighth molecular solution, etc. Solutions that have the same number of gram-molecules of various substances dissolved in the unit volume are *equimolecular.*

It is at once apparent that, if the dissolved substances do not undergo any change on being dissolved, the same number of dissolved molecules are present in all equimolecular solutions. When we employ equimolecular solutions in pharmacological study we are, therefore, able to compare the behavior of a definite number of the molecules of one substance with the behavior of the same number of another substance.

We can illustrate the advantages of employing such molecular solutions in pharmacological study in place of percentage solutions, in the following way: It is ordinarily stated that, of the three salts, potassium bromid, sodium bromid, and lithium bromid, the last-named acts more

powerfully than the other two. This is on the basis of equal amounts *by weight* of the three substances being given (say in 10 per cent. solutions). When we compare the molecular weights of these three substances (which stand to each other as 119.11, 103.01, 86.99), the reason for this apparent inequality in action becomes evident. The chief physiological or therapeutic effect of these three bromids resides in their bromin content, and (roughly) a 12 per cent. solution of the potassium salt is required to furnish the same amount of bromin as a 10 per cent. solution of the (anhydrous) sodium salt, or an 8.7 per cent. of the lithium salt. Or, to apply this to daily practice, when we substitute a gram dose of lithium bromid for a gram dose of potassium bromid, we are giving a third more of the active constituent of our drug.

For certain purposes in pharmacological study it is well to employ *normal solutions.* A normal solution is a gram-molecular solution, provided the dissolved substance is monobasic. In other words, the power of the substance to displace hydrogen is taken into consideration. So a normal solution of hydrochloric acid contains a gram-molecule (36.46 grams) of the pure acid in the liter of finished solution. But to get a normal solution of the dibasic sulphuric acid, only 49.04 grams, that is to say, only one-half the molecular weight (=98.08), are used; or of the tribasic phosphoric acid, only 32.67 grams (=1/3 its molecular weight, 98.02). Similarly, a normal solution of sodium chlorid (molecular weight, 58.5) contains 58.5 grams in the liter of solution, while a normal solution of trisodium phosphate ($Na_3PO_4 . 12H_2O$, molecular weight, 380.34) contains only 126.78 grams. Clearly, therefore, the familiar normal solutions of the chemists are the same as the molecular solutions more commonly employed by the physiologists, *provided* monobasic acids or salts are involved. But, if polybasic substances are under consideration, then a normal solution of a dibasic compound has only half the concentration of a molecular solution of the same compound; a normal solution of a tribasic compound only one-third the concentrations of a molecular solution of this same substance, etc.*

A third basis upon which the solutions of various substances must at times be standardized is that of their *ionic concentration.* When the electrolytes go into solution in water they become dissociated, as we found above. But the degree of dissociation is not the same for all electrolytes, and under all conditions. So, for example, if we take a series of equinormal acids, the number of hydrogen ions in these is by no means the same. Strong acids, such as hydrochloric, nitric, or sulphuric, will in

* The "physiological salt solution" or "normal salt solution" of our physiological laboratories, hospitals, etc., has absolutely nothing to do with the normal solutions being discussed here. The terms are misnomers and mean nothing, and should disappear from use. We should speak of an 0.85 per cent. or 0.9 per cent. sodium chlorid solution, if that is what we mean by these terms.

dilute solution be almost entirely dissociated, but the weak acids, such as acetic or carbonic, will be dissociated only very little. Suppose, now, that we are trying to determine the relative value of different acids in the digestion of the proteins under the influence of pepsin. It is not sufficient under such circumstances to work only with equinormal acid solutions. It is also necessary to work with solutions that have the same ionic concentration. For the methods employed in the preparation of such solutions the larger textbooks of physical chemistry must be consulted.

EQUILIBRIUM

Living matter represents nothing but a series of physicochemical reactions of such a nature that the materials necessary for these reactions are sought by the living matter (that is, by certain of the physicochemical reactions themselves), while at the same time the products of these physicochemical reactions, which if allowed to accumulate would bring the whole series to a stop, are properly disposed of, the sum total of reactions being accomplished in such a way that the system in which these reactions are taking place (living matter itself) undergoes no marked changes over long periods of time. What is meant by a long period of time is simply a matter of definition; in the case of some of the insects it may be but a few hours; in some of the higher animals a century. The maintenance of the system constitutes physiology and normal life; every interference with it, pathology and disease. The purpose of preventive medicine is the maintenance of the former; the purpose of therapy the relief of the latter, and its restoration, if possible, to the former. The whole is governed by the laws of equilibrium (11).

We can best see what all this means in the case of man if we consider the ameba. The ameba lives in a state of equilibrium with its surroundings. If we take it out of its pond and put it in distilled water it dies. If we put it in a strong salt solution it dies, or if we keep it in its own pond water, but cover this so that no air can get to the surface of the water and into solution in the water, it dies. The grosser reasons for all this are easily given. Pond water contains besides water certain salts and oxygen. The water in the organism is in equilibrium with the water in the pond; the salts in the organism are in equilibrium with the salts in the pond water; the oxygen dissolved in the protoplasm is in equilibrium with the oxygen dissolved in the pond water. To put the ameba under any of the conditions mentioned above is to change one (or indirectly several) of these equilibria, and, if any of them is sufficiently changed, then that normal system of physicochemical reactions that we call life is disturbed, maybe to the point of cessation. In the distilled water the ameba loses its salts down to a fatal point; from the concentrated salt

solution it absorbs more of these than the physicochemical reactions can stand; when the entrance of oxygen into the water is rendered impossible, then none gets into the living ameba, and so its normal oxidative processes are interfered with, and it dies.

We can, on the other hand, kill our ameba by furnishing it the pond water, but by placing it in a position which does not permit it to rid itself of the products of its physicochemical reactions. So, if we allow the water to get stagnant, it will die. Under these circumstances the carbonic acid and other products of its activity accumulate in the water about the ameba, and in the ameba itself, and, as the organism cannot bear more than a certain concentration of these products, it dies.

The extremes between which our ameba is able to still maintain itself (minimal salt concentration, minimal oxygen concentration, maximal carbonic acid concentration) are highly important for its life—they constitute the measure of *the resistance* of the organism to such conditions.

What has just been said continues to hold true, if, without changing another word, we write brain cell, or muscle cell, or connective tissue cell in place of the term ameba in what we have been discussing. For pond water we may substitute the term blood, or lymph; in place of oxygen above the water we may say the air in the lungs; in place of stagnant water we may say sweatshop atmosphere. Every cell in the multicellular organism is in the same situation as the ameba, and as dependent as this upon the liquid medium that surrounds it. If we bear these points in mind, the physical chemistry of a therapeutics that urges water, a proper salt ration, the out-of-doors life, and a ventilated shop system upon us at once becomes clear. These are the everyday illustrations of the laws of equilibrium that are ordinarily only murmured within the walls of the laboratory.

We shall illustrate this matter of equilibrium a little further: Suppose we have any vessel partially filled with water, and above this any gas, such as oxygen. This oxygen will go into solution in the water up to a certain point, when no more will be dissolved. If now we increase the pressure of oxygen in the space above the water, then more of the oxygen goes into solution; or, if we reduce this pressure, some that has gone into solution will again escape. The process is, therefore, *reversible*. For any given pressure of the gas there is always a certain amount of this gas dissolved in the water. In other words, the dissolved gas is always in equilibrium with the gas above it. We represent this as follows:

$$\underset{\text{(Gas)}}{\text{Oxygen}} \rightleftarrows \underset{\text{(Dissolved in the water)}}{\text{Oxygen}}$$

But let us suppose that a substance capable of combining with the oxygen is dissolved in the water. As the dissolved oxygen combines

with this substance, the concentration of the dissolved oxygen must be reduced, and so the previously established equilibrium is destroyed. In consequence of this more of the oxygen above the water must now be taken up, and this continues until the whole system, in which we now have to consider three elements, is once more in equilibrium. In other words:

Oxygen		Oxygen		Oxygen
(Above the water)	$\rightleftarrows$	**(Dissolved in water)**	$\rightleftarrows$	**(Combined)**

As a matter of fact, this is exactly what occurs in the blood when it passes through the lungs. The oxygen pressure in the alveoli of the lungs being higher than that of the oxygen dissolved in venous blood, the oxygen passes from the alveoli into the blood. But hemoglobin is found in the blood, which is capable of taking up large quantities of oxygen (12), in consequence of which the equilibrium existing between the oxygen in the air and the oxygen dissolved in the blood plasma is broken down in the direction toward the hemoglobin, and so more oxygen is taken up by the plasma. And this continues until an equilibrium exists in the three phases involved, thus:

Oxygen		Oxygen		Oxygen
(In alveolar air)	$\rightleftarrows$	**(Dissolved in plasma)**	$\rightleftarrows$	**(Combined with hemoglobin)**

When this arterial blood gets to the tissues it meets a region in which the oxygen pressure is lower than that in the blood, and so the dissolved oxygen in the plasma moves over into the body cells. In consequence of this the hemoglobin now gives up its oxygen to the plasma, and this process continues until equilibrium is again restored.

Entirely analogous conditions prevail in the case of carbonic acid, and the loss of the carbon dioxid from the lungs. The carbonic acid is produced in the cells, and passes over into the blood plasma which passes by these cells and in which the concentration of carbonic acid is lower than in the body cells. As soon as the carbonic acid gets into the blood plasma it begins to combine with the carbonates present here and makes bicarbonates out of them. The carbonates behave in this regard toward carbonic acid as hemoglobin did before toward oxygen. The state of equilibrium that tends to become established in the tissues may be represented as follows:

H_2CO_3		H_2CO_3		H_2CO_3
(In the cells)	$\rightleftarrows$	**(Dissolved in the plasma)**	$\rightleftarrows$	**(In combination with carbonates)**

When the venous blood gets to the lungs, where the CO_2 tension in the alveoli is low, the CO_2 of the carbonic acid found in the plasma escapes

(water remaining behind in the blood). As this happens the bicarbonates break down and give up a part of their carbonic acid to the blood plasma, and this continues until equilibrium is again restored.

A classical example of purely *chemical equilibrium* is furnished by the combination of ethyl alcohol with acetic acid. If at a definite temperature chemically equivalent amounts of acetic acid and ethyl alcohol are mixed together, a reaction ensues according to the following equation,

$$\underset{\text{(acetic acid)}}{CH_3COOH} + \underset{\text{(ethyl alcohol)}}{C_2H_5OH} = \underset{\text{(ethyl acetate)}}{CH_3COOC_2H_5} + \underset{\text{(water)}}{H_2O}$$

The reaction takes place in the direction from left to right. If, now, we mix together chemically equivalent amounts of ethyl acetate and water, ethyl alcohol and acetic acid are formed. In other words, the above reaction takes place from right to left. Neither in the first nor in the second instance does the reaction become complete. Before the given amounts of acetic acid and ethyl alcohol, or ethyl acetate and water, have undergone complete decomposition, the reaction comes to a standstill. Such a reaction which can take place from right to left as well as from left to right is called a *reversible reaction.* We indicate this as we have done above in the case of oxygen and carbonic acid as follows:

$$CH_3COOH + C_2H_5OH \rightleftarrows CH_3COOC_2H_5 + H_2O$$

It can be readily seen that, when equilibrium is established in a reversible reaction, the four substances reacting with each other are present in the reaction mixture. The characteristic feature of such a condition of equilibrium is found in the fact that under the same external conditions it is always the same, no matter from which side it is reached. In other words, it is immaterial whether chemically equivalent amounts of acetic acid and ethyl alcohol or chemically equivalent amounts of ethyl acetate and water are mixed together. The condition of equilibrium is in the end the same in either case.

Although we say ordinarily that when equilibrium has been established the reaction has come to a standstill, this is really incorrect. When equilibrium has been established between the two sides of an equation it really means that the chemical changes are still going on, only the amount of change in the one direction is exactly counterbalanced by the reverse change in the opposite direction. The reaction is, therefore, *stationary.*

What happens if after equilibrium has been established we introduce into the reaction mixture either ethyl acetate or acetic acid and alcohol, or remove either of these from the amounts that are present? Clearly this must disturb the existing equilibrium, and, depending upon the side

upon which this disturbance has taken place, more ethyl acetate and water must be formed, or more ethyl alcohol and acetic acid.

Upon the operation of these laws of equilibrium depend not only all the processes of normal absorption and secretion by the living animal, but all those of abnormal absorption and secretion that are better known to us under the headings of *intoxication,* and its reverse, *detoxication.* How to prevent the former, and how to aid the latter, constitute two cardinal problems in therapy.

DIFFUSION

If we very carefully pour some distilled water upon a concentrated solution of copper sulphate, the colored layer does not immediately mix with the clear water above it. If we set the apparatus aside in a quiet place and watch it, we notice that the blue color gradually spreads upward through the clear water until in the end the whole vessel contains a uniformly blue solution. The dissolved particles of copper sulphate spread upward into the clear water by a process of *diffusion.*

To return once more to our ameba in its pond water (which we have made analogous to the individual cells composing man surrounded by their blood and lymph), we can say that all the substances necessary for the life of this ameba, or the various poisons that may be added to the pond water to injure or kill the ameba, get from the pond water into the organism by a similar process of diffusion. Conversely, the poisonous products formed by the ameba in its daily life, or the substances which have accidentally found their way into the organism and are capable of acting as poisons, can get out of the ameba into the surrounding medium (and so be swept away) only through this same property of diffusion.

We have already discussed how important a part the laws of equilibrium play in this process of diffusion. Diffusion is possible only because the distribution of the dissolved substances in the system under discussion is not of such a character as to have the whole in equilibrium. Food substances, oxygen, and poisons diffuse into the living ameba because the concentration of these within the ameba is less than that necessary to establish an equilibrium between these substances as found here and the same substances found in the pond water. Similarly, the various poisonous products and many of the normal constituents of protoplasm, notably the salts, diffuse out because the concentration of these in the pond water is less than sufficient to be in equilibrium with these same substances as found in the protoplasm of the ameba. Upon the maintenance of a proper concentration of food supply, medicinal agent, or poison in the pond water (or blood and lymph) depend in the first instance proper nutrition and adequate therapy, or an intoxication. Upon the maintenance of a sufficiently low concentration of the involved substances in the second

case (circulation of fresh water about the ameba, administration of water to a poisoned man) depends the removal of the poisonous substances from the intoxicated cell, while there resides in this good therapeutic procedure the danger at the same time of injuring the involved cells by allowing the diffusion out of them of some of their normal constituents.

We have now to consider some of the factors that modify the problem of diffusion as this operates in the living animal. Thus far we have entirely ignored the *time factor,* and, secondly, the fact that living cells are more than mere isolated drops of water. In other words, the nature of the diffusing substances and the constitution of protoplasm affect this process of diffusion as originally described in our cylinder of water, at the bottom of which we had placed a concentrated copper sulphate solution.

We have already touched upon one great classification of the various substances that are concerned in the physiological and therapeutic aspects of this problem of diffusion. The state in which a chemical compound exists affects its diffusion behavior. The colloids we noted above scarcely diffuse at all when compared with the way in which crystalloids diffuse. Herein, for example, resides one of the great purposes of digestion. Through digestion the colloid proteins, carbohydrates, and fats are changed into compounds that are crystalloidal in character, and so from a state in which they practically cannot diffuse into living cells to one in which they do this promptly.

But even among the crystalloids the rate at which diffusion occurs is by no means the same. The diffusion velocity of sodium chlorid, dextrose, and magnesium sulphate decreases in the order named. Similarly, the rate of diffusion of these substances into cells (their absorption) decreases in the order named (13).

Along with these specific differences in the rate of diffusion of different dissolved substances we have to remember that, if we are dealing with a mixture of diffusing substances, the one may modify the rate of diffusion of the other, as this would have appeared had it alone been in solution (Arrhenius, 14).

Another factor that influences this problem of diffusion as observed in living matter resides in the fact that protoplasm is not a pure solvent (water), but a colloidal mass. It used to be held that diffusion occurs just as readily into and through such a colloidal mass as gelatin or agar-agar as into and through pure water, but this is not strictly true. The presence of colloidal material retards the rate of diffusion of dissolved substances, and this the more, the higher the concentration of the colloid in the medium into which diffusion is occurring (15). Or, to apply this to the problem of pharmacology, a dissolved substance will enter the protein portions of a cell less rapidly than pure water; or, if different cells are involved, it will enter most rapidly into those which are richest in water. Now, since the water capacity of any tissue cell varies under

physiological and pathological conditions (normal water content and edematous state), it is evident that corresponding herewith substances may diffuse into cells more rapidly at one time (say in certain diseases) than at another.

DISTRIBUTION

Thus far our argument has shown us that diffusion occurs from a region of higher concentration to one of a lower concentration, and has seemed to indicate that this will go on until the concentration of each of the diffusing substances is the same everywhere. In other words, it has seemed as though the attainment of a state of equilibrium is synonymous with equality of distribution.

So, for example, in our ameba we have made it appear that equilibrium would be established between the ameba and the pond water surrounding it as soon as the concentration of every dissolved substance in the two phases is the same. The same would hold true of the individual cells of the multicellular organism. So we might suppose that after a dose of potassium iodid or strychnin or alcohol to a patient, equilibrium would be attained as soon as the distribution of these various drugs was the same in all the tissues and fluids of the body.

Actually we know that nothing of the sort occurs. In fact, we know that a uniform distribution of any dissolved substance throughout the cells and fluids of a living organism probably never occurs. So the concentration of the various salts in the ameba is not that of these same salts in the pond water; and the potassium iodid, the strychnin, and the alcohol distribute themselves very unequally through the multicellular organism. The iodids are likely to accumulate in the thyroid; the strychnin in the spinal cord; the alcohol in the brain. These inequalities in distribution are pointed to by men who believe that we shall never be able to interpret all life phenomena on a purely physicochemical basis as evidences indicating that living matter has "peculiar" properties not known to the physical chemist in his study of "dead" material. Such pessimism is at least premature. As the following shows, we are already in a position that permits us to account very easily for a large bulk of these phenomena.

1. Inequalities in Distribution Due to Inequalities in Solubility

When we take a solution of iodin in water and cover this with a little ether and shake the whole, we can see even from naked eye appearances that the iodin is ultimately present in very unequal concentrations in the two liquids. While scarcely any color remains in the water, the ether shows a deep coloration with iodin. The process is a homely illustration

of the everyday chemical procedure that we call "shaking out with an immiscible liquid." The extraction of the iodin from the water by the ether depends upon the fact that iodin is soluble in the ether, and, in the example cited, the solubility of the iodin is so decidedly greater in the ether than in the water that practically all the iodin moves over into the ether phase. The ultimate state of equilibrium attained, which is characterized by this very unequal partition (distribution) of the dissolved substance between the water phase and the ether phase, is in this case due to the difference in the relative solubilities of the iodin in the water and in the ether. As the iodin is more soluble in ether than in water, most is ultimately found in the ether phase. If we take equal volumes of water and ether, and drop into the mixture a measured amount of iodin, say a gram, we find, when equilibrium has been attained, that (roughly) one-tenth of this has dissolved in the water and nine-tenths in the ether. If we use instead two grams of iodin, we have again the same proportionate distribution of the iodin, one-tenth of the amount added goes into the water, and nine-tenths goes into the ether. And this result is constant, no matter whether we first mix the water and the ether and then add the iodin, or whether we dissolve the iodin in the ether and then add the water, or vice versâ. In the end the state of equilibrium attained is always the same. The proportion of iodin dissolved in each of the two phases—in this case a concentration of iodin nine times as high in the one as in the other—is always constant. We call this the *distribution coefficient* or *coefficient of partition* (16).

In our discussion of the living cell so far we have spoken of its solvent powers for various substances chiefly from the standpoint of its water content. If the cell had solvent powers only so far as its water content is concerned, it is obvious that dissolved substances could never appear in it in higher concentrations than those of these substances in the media surrounding the cell. But this conception of the cell is too limited. In addition to water, the various cells of all living organisms contain fat and fat-like bodies. The latter are called lipoids, and include such substances as cholesterin, lecithin, protagon, and cerebrin. We can see in advance, therefore, that the living cell must be able to take up (that is, dissolve or absorb) many substances that are better soluble in such fats and lipoids than in water, in greater amounts than the media surrounding these cells which are less rich in, or devoid of, these substances.

We are indebted to Hans Meyer (17) and to E. Overton (18) for recognizing the great physiological and pharmacological importance of the facts here outlined. (The distribution law of Berthelot and Jungfleisch, 16.) By methods which we need not discuss here, these authors found it possible to differentiate between substances which pass into or through cells very slowly, and those which pass rapidly.

To the compounds which diffuse rapidly into protoplasm belong the

monatomic alcohols, aldehydes, and ketones, the hydrocarbons with one, two, and three chlorin atoms, the nitroalkyls, the alkylcyanides, the neutral esters of inorganic, and many organic acids, anilin, etc. The diatomic alcohols and the amids of monatomic acids pass into cells more slowly; and still more slowly glycerin, urea, and erythrite. The hexatomic alcohols, the sugars with six carbon atoms (hexoses), the amino acids, and the neutral salts of the organic acids diffuse into cells only very slowly (Overton, 18).

A simple glance at the list just given shows that we have to deal here with all manner of chemical substances. Some of these are relatively simple in composition, some very complex; some are of physiological importance, and are found as normal constituents of the living cell; others are entirely foreign to the living organism. What physicochemical character have all these substances in common, which allows them to penetrate living cells with more than usual ease, and so to stand out from the great group of the ordinary neutral salts, for example, which can penetrate the cells only much more slowly?

An explanation frequently given and long believed to be the correct one is that the size of the molecules is the condition which determines the entrance of the dissolved particles. According to this conception, the cell protoplasm as a whole, or the "membranes" (to be discussed later) believed by many (including Overton) to exist about cells, are regarded as sieves which allow all molecules that do not exceed a certain size to pass into the cell, while those larger than this are held back. The deficiencies of any explanation which calls for the existence of membranes about cells we will point out later, but even now it must be apparent that the sieve-like behavior attributed by some authors to such membranes or to protoplasm as a whole lacks all support, for cells which readily give passage to such large atomic aggregates as the alkaloids and sodium salicylate hold back the much simpler amino acids and potassium sulphate.

The substances enumerated above enter cells because the cells contain substances which in their properties as solvents behave not unlike ether. All those compounds which are more soluble in ether (and other oil-like bodies) than in water must, therefore, pass into and through cells containing ether-like solvents (fat, cholesterin, lecithin, cerebrin, protagon), more rapidly than into and through such as do not contain such solvents; and with a given cell the rapidity and the absolute amount of any compound ultimately taken up must depend upon the relative degrees of solubility of the substance concerned in water and in the ether-like bodies contained in the cells (distribution coefficient). In other words, it depends upon the distribution coefficient of the dissolved substance between the two phases (water and ether-like bodies) whether any dissolved substance will enter a cell slowly or rapidly, and whether

it will ultimately be found in the cell in a greater, in the same, or in a lower concentration than in the medium surrounding it.

With these ideas in mind, it is only necessary to reëxamine the list of substances which experiment has shown enter cells with more than usual velocity, and see if they are not all of them of a character which renders them more soluble in ethereal or oily substances than in water, and if those which stand first in the list and consequently enter cells most rapidly are not such as have the highest distribution coefficients in favor of the ethereal or oily substances. An illustration or two may make this clearer. The repeated substitution of an atom or a group of atoms for some other atom or group of atoms in a chemical compound is often accompanied by marked changes in the solubility of the compound and its derivatives. Glycerin enters a cell only very slowly. When an atom of chlorin is introduced into this compound, the new compound obtained enters protoplasm more rapidly, and, when two are introduced, still more rapidly, for these derivatives are more readily soluble in fats than the original glycerin. The same holds true of urea and its methylated derivatives. While urea diffuses but slowly into cells, the introduction of one, two, or three methyl radicals into this compound increases progressively its solubility in fats, and also the rate of diffusion into living cells.

The tremendous pharmacological importance of these simple facts is self-evident. In order that a substance may produce any physiological effect, it must first get into the cell. Other things being equal, we may therefore expect a quicker and a more powerful effect from a lipoid-soluble pharmacological preparation than from one that is not thus soluble (19). Upon this depends a whole chapter in the chemistry of pharmacological preparations, in which some pharmacologically active compound, which in itself gets into cells only slowly and so is not very active, is made active by being introduced into some compound which is more readily soluble in the lipoids.

The marked effect of all the anesthetics (chloroform, ether, alcohol, ethyl chlorid), and the various alkaloids (morphin, cocain, atropin), is associated with the fact that they are lipoid-soluble. Their great effects upon the central nervous system are in large measure associated with the fact that nervous tissues are rich in fat and fat-like bodies, and so these tissues take up these substances with special avidity. We can appreciate also why a fat individual demands more anesthetic before going to sleep than does a lean one. Anesthesia, like all intoxication, is a matter not of absolute amount present, but of concentration. The various grades of anesthesia go hand in hand with definite concentrations of anesthetic in certain cells of the central nervous system. It must evidently take longer to attain this concentration in a fat man than in a lean one, for the ready solubility of the anesthetics in fat means that the

ordinary fat-containing cells of the body must be saturated with anesthetic at the same time that we are trying to do this to certain cells in the central nervous system. And so a greater initial absolute amount of anesthetic must be taken up by a fat individual than by a leaner one.

2. Inequalities in Distribution Due to Inequalities in Adsorption

Not only may a living cell come to contain in the unit volume a greater amount of a dissolved substance than does the surrounding medium because the cell contains better solvents for the dissolved substance than does the surrounding medium, but it may take up an unexpectedly large amount because of its *adsorptive* powers. These adsorptive powers are associated with the fact that the cell is largely colloidal in its make-up. The general problem of adsorption may be illustrated as follows (20):

If we dissolve a dye in distilled water, we get a uniformly colored solution. If, now, we divide the solution into two parts, and add to the one a little finely powdered charcoal and then shake both, we find after a little time that, while our control solution remains entirely unaltered, the color has very largely disappeared from the other. We are not dealing here with a chemical reaction,—the pure carbon that we added to the colored solution does not react chemically with any of the constituents in the tube. The powdered charcoal has a great surface, and the action of this great surface upon the dissolved particles of the dye has made this accumulate (condense) upon the surface of the charcoal. The theory of how this surface action is accomplished need not interest us here.

What has been described is an example of *adsorption*. The charcoal used in the experiment is the adsorbent; the dye the adsorbed substance.

An enormous number of substances could be cited as acting under various conditions as such adsorbents; and almost any substance could be given as an example of a material capable of being adsorbed. Kaolin, finely divided precipitates of all kinds, or any of the inorganic or organic colloids may take the place of carbon in the above experiment, and acids, alkalies, and salts can be adsorbed in the same way as our readily visible dye. Examples of adsorption are familiar to everyone. The chemical decolorization of beers, sugars, etc., under the influence of animal charcoal; the removal of color from a bath by dipping wool, cotton, etc., into it (dyeing); the staining of histological specimens, are all examples of adsorption.

The adsorption of any substance by an adsorbing agent is never complete. In the case of a dye and charcoal, it is never possible to take all of the dye out of the bath with the charcoal,—a little always remains behind. In other words, the distribution of the dye between the solvent

and the adsorbent is governed by the laws of equilibrium. If, after we have had the charcoal take as much of the dye out of the solution as is possible, we pour off the supernatant liquid and substitute pure water for it, then some of the dye will leave the charcoal and go back into solution in the water. In this way we can again wash all the dye out of the charcoal. Conversely, if, after we have had the charcoal take up as much dye as possible, we add more dye to the supernatant liquid, then the charcoal will proceed to take up an additional amount from that which we have added.

The relationship between the concentration of the substance to be adsorbed and the amount taken up by the charcoal is an interesting one, and may be thus stated: From relatively dilute solutions the adsorbent will take up much; from more concentrated solutions relatively less, of the substance to be adsorbed. In other words, if at a certain concentration we can take four-fifths of the dye present in a solution out of this with a given amount of charcoal, then, if the dye has a higher concentration, we can take out only less than four-fifths, or, if it has a lower concentration, more than four-fifths.

Protoplasm behaves toward substances dissolved in a medium that surrounds it in an entirely similar way. This constitutes another reason why protoplasm may contain the same, a higher, or a lower concentration of any dissolved substance than the medium surrounding it. The protoplasm (adsorbent) of different cells behaves differently toward the same external conditions, and so it comes to pass that, while all cells are bathed with essentially the same blood and the same lymph, they do not all adsorb the same amount of the proffered materials. In other words, equilibrium is not attained between the protoplasm of different cells and the medium surrounding these, at exactly the same point. Hence it happens that the salt content of different cells is not only not the same under physiological conditions, but, if we offer the cells of the body any pharmacological preparations (say an iodid), all the cells of the body will not take this up equally. So the thyroid, for example, because of its peculiarly high adsorbent powers for the iodids, will be found particularly rich in iodin after medication with this drug; iron will tend to collect in the liver and the mammary glands, etc.

The adsorption properties of protoplasm are markedly influenced by various external conditions (21). If we alter the reaction of the medium in which protoplasm finds itself (say from the normally neutral to an acid one), then the adsorption powers change most markedly. Thus a given tissue which under normal circumstances proved an excellent adsorbent for certain dissolved substances may practically lose this, or conversely, a tissue which before adsorbed a given substance only poorly may now take this up with avidity. The pharmacological import of this is easily seen. The former is equivalent to a defective adsorption, the

second to an abnormally good one. The maintenance of a normal physiology (absorption of food) depends upon the former, or the proper absorption of a pharmacological preparation. Loss of adsorption power may, therefore, be followed by serious consequences. On the other hand, an increased adsorption power may be equally dangerous, for a pharmacological preparation which is absorbed but little by a given healthy tissue may in disease be absorbed so well that it produces unexpectedly powerful effects.

3. Inequalities in Distribution Due to Specific Chemical Differences

A third reason why a cell may contain substances in a higher (or lower) concentration than the medium surrounding the cell resides in the fact that the cell may contain substances capable of combining chemically with the proffered dissolved substance. So, for example, if a cell contains iron, it is reasonable to expect in advance that this cell will take up more of a proffered poison capable of combining with the iron (say a ferrocyanide) than a cell not containing iron, or iron in less amount. We need not multiply such illustrations, for the list is as long as the list of chemical reactions capable of ensuing between the various substances found in any living cell and the substances that come normally or abnormally in contact with this cell.

All the "specific" effects of various pharmacological preparations of "toxins," of "ferments," etc., and the "specific reactions" of protoplasm due to these, are generally regarded and might be used in illustration of such inequalities in distribution, as we are here discussing (22). This point of view is, in the main, correct. But it is likely to be carried too far. We are still too strongly under the influence of the "purely chemical" point of view in this matter. We have already learned that many of the "specific immune reactions" are not so intensely "specific," and the whole realm of colloid chemistry is dotted with examples of reactions that have been looked upon as "chemical" in character when further analysis has shown that what was considered "specific" in these reactions did not depend upon the presence of certain chemical compounds, but rather upon the physical states in which the components of the reactions entered into these.

4. Inequalities in Distribution Due to Interference from "Membranes"

Were we to sum up in a few words our conception of the structure of protoplasm as thus far developed, we could liken it fairly accurately to a mass of gelatin (protein) intimately mixed with more or less fat-like

material (the fats and lipoids), the whole being under physiological conditions immersed in a liquid (pond water in the case of our ameba, or lymph and blood in the case of our body cells), from which the protein-fat mixture soaks up a certain amount of water as well as the various dissolved substances found in this water. What governs the matter of water absorption we shall have occasion to discuss shortly. The absorption of the dissolved substances we have made a matter of equilibrium between the medium outside the cell and the medium which constitutes the cell, and we have indicated how the solubility characteristics, the phenomena of adsorption and chemical combination, influence the point at which equilibrium is reached. This simple picture of the cell furnishes to our minds an adequate conception of its main structure.

But this is not the conception of the cell which all, or even the majority, of biological workers accept as correct. Since the studies of W. Pfeffer and Hugo DeVries it has been generally held that both plant and animal cells have "membranes" (osmotic membranes or semipermeable membranes) about them (23). This is a teaching which we believe incorrect. The question is discussed in greater detail later, but it is brought up here because, if such membranes existed about cells, they would be an additional factor in determining the distribution of dissolved substances between cells and their liquid surroundings.

The original teachings of Pfeffer and DeVries held the membranes about cells to be entirely analogous to the osmotic membranes (the so-called semipermeable precipitation membranes) of the physical chemists. Such membranes are freely permeable to the solvent (water), but impermeable to substances dissolved in the solvent. Did such membranes exist about cells, it is therefore clear that water could freely pass into and out of cells, but the substances dissolved in the water surrounding the cells could not get in, and those in solution within the cell could not get out.

On the face of things, it is evident that such a conception cannot be wholly correct, for, if cells had true semipermeable membranes about them, no food materials could ever get into them, no products of metabolism get out, and this would mean death. So, for these true semipermeable membranes the more modern school has substituted such as are partially permeable, and very complicated these are (24). As we do not think that any such complicated structures exist, we shall not discuss them further. We only wish to emphasize the fact that, should such membranes ultimately be shown to exist about cells, they will be capable of maintaining concentration differences (at least for shorter periods of time) between the dissolved substances within the cell and those without, for, if a membrane is permeable only to some dissolved substances, then those which cannot pass through may accumulate in unusual quantities either within or without the cell.

THE PHARMACOLOGICAL IMPORTANCE OF THE THEORY OF ELECTROLYTIC DISSOCIATION

In the earlier portions of this chapter it was found that the crystalloids can be divided into two great groups, the electrolytes and the non-electrolytes. When the electrolytes go into solution in water we find them to undergo dissociation, so that ions result. When we deal with the effect upon protoplasm of various electrolytes dissolved in water, do we deal with the effects of the molecules of these electrolytes, or with the effects of the various ions which these yield on solution? So far as the pure chemistry of the electrolytes is concerned, we know that their behavior is determined, in the main, by the ions they yield on solution. So, for example, the various group reactions that we are familiar with in chemistry are now known to be essentially reactions between ions of the same kind. The reason that all acids taste sour, redden litmus, and attack metals is that on solution in water all acids yield hydrogen ions—the property that all acids have in common. Alkalies, on the other hand, have an alkaline taste, turn litmus blue, etc., because all have hydroxyl ions in common.

The specific differences between different acids arise from the fact that the radicals united with the hydrogen in the molecular acids are different, and when dissolved in water these form different kinds of ions. So hydrochloric acid and nitric acid, when dissolved in water, are the same in that both yield hydrogen ions, but different in that the one yields chlorin ions in addition, while the other yields NO_3 ions. Similarly, the specific differences between the bases are to be sought in the specific differences between the metals with which the hydroxyl in the base is combined. On solution in water the bases are all the same in that they yield hydroxyl ions, but different in that sodium hydroxid yields in addition sodium ions, potassium hydroxid potassium ions, and calcium hydroxid calcium ions.

When silver nitrate is added to a mixture of different salts, all the chlorids are precipitated. This is because all the chlorids on solution in water yield chlorin ions, and the silver ions of the silver nitrate react with these and produce a precipitate. When silver nitrate is added to a substance in solution which contains chlorin, but not in a form which makes this appear as chlorin ions, no such precipitate is formed. Thus silver nitrate does not precipitate the chlorin from a chlorate, for this does not yield Cl ions as does the chlorid, but ClO_3 ions; nor the chlorin out of chloroform which is a non-electrolyte, and therefore yields no ions at all.

When we deal with the effects of the various acids, bases, and salts upon protoplasm, in other words, with the effects of these various elec-

trolytes, do we deal with the effects of the various molecules of these compounds or with the effects of the various ions that these yield in solution? In greater part we deal with the effects of the various ions that these yield.

The first proof of the truth of this statement was brought by H. Dreser (25), and in the field of pharmacology. Dreser was working with the effects of different mercury salts, and showed that their toxic action was primarily a function of the mercury ions they yield on solution in water. When the toxic effect of solutions of different mercury compounds containing the same amount of mercury in the unit volume are compared, it is found that, in spite of this fact, they have a very different degree of toxicity. Thus mercury sulphocyanate is more toxic than mercury cyanide, and this more toxic than mercury thiosulphate. While all these compounds yield mercury ions when dissolved in water, they yield an unequally great number. Corresponding to the fact that the first yields the largest number, it is found to be most toxic.

The next evidence in this direction was brought by Grützner (26), who showed that the toxic effect of various acids on nerves was chiefly a function of the hydrogen ions the acids yield, and that the degree of toxicity of different acids parallels (roughly) the degree of dissociation of the acids; in other words, the concentration of the hydrogen ions. Kahlenberg and True (27) brought out the same fact in studying the effect of various acids, bases, and salts on the growth of sprouting beans. These authors found that such sprouting beans will just live in solutions of the strong acids (HBr, HCl, HNO_3, H_2SO_4) when a gram-molecule of these substances is dissolved in 6,400 liters of water. In solutions as dilute as this, dissociation into ions is complete, and there are no longer present any molecules of the acid. Hence, the toxic action cannot be due to the molecules of acid. The toxic action can therefore be due only to the hydrogen ions, or to the different acid ions, or to these together. No toxic effect is shown by a sodium chlorid solution, which is equimolecular with a toxic hydrochloric acid solution, and, since such a sodium chlorid solution yields just as many chlorin ions as the acid solution, the toxic effect of the acid solution cannot be due to the chlorin ions. It must, therefore, be due to the hydrogen ions.

By similar methods it can be shown that the toxic effect of hydroxids is chiefly a function of their hydroxyl ions. Sodium chlorid solutions having a concentration equivalent to toxic sodium hydroxid solutions are non-poisonous. Since both contain sodium ions and in the same concentration, and since the hydroxid solution is toxic at a concentration when dissociation is complete, the toxic effect of the sodium hydroxid must be due to the hydroxyl ions.

In the same way J. Loeb (28) has shown that the loss of irritability of a muscle and the amount of water this absorbs in an acid solution is

a function of the ions of the acid concerned; Richards (29) has shown that the taste of acids, alkalies, and salts is dependent upon the ions they yield; Kahlenberg and True, Paul and Krönig (30), and Scheurlen and Spiro (31), that the antiseptic action of various metallic salts (mercury, silver, gold) is determined in the main by the ions they yield, and is the greater the higher the number of poisonous ions yielded.

Since these earlier papers an enormous literature has sprung up around this general subject of the physiological effects of ions (32).

THE EFFECT OF VARIOUS EXTERNAL CONDITIONS ON THE COLLOIDAL STATE

Our discussion thus far has brought us to a realization of the fact that the reactions which characterize the living cell occur in a colloidal medium; it has further indicated the means by which various dissolved substances get into and out of this colloidal substance. We have now to discuss the relation of these two to each other; in other words, the action of the various substances which manage to get into or are produced in and fail to get out of a cell upon this colloidal matrix, and conversely, the effect of the matrix upon the substances dissolved in it.

We can sum up the problem involved from our special viewpoint by discussing *the effect of various external conditions upon the physical state of colloidal material* (33). What is said under this heading may then with slight or no modification be directly applied to living protoplasm. We shall choose for special discussion the effects of a limited number of external conditions that are of interest because of their bearing upon pharmacology and therapeutics.

All colloids, including those found in the living animal, are conveniently classed, as we found above, into suspension colloids and emulsion colloids. This classification is made, as was pointed out, on the basis of the relationship that exists between these colloids and the solvent in which they find themselves. The suspension colloids are not so intimately associated with their solvent as are the emulsion colloids. While we can readily separate the solvent from the colloid in the first case, this is done only with great difficulty in the second. It is possible, for example, to separate in some suspension colloids (the colloidal metals) the solvent from the colloid by suitable methods of filtration; in the emulsion colloids no such simple procedures suffice. If we take a swollen piece of gelatin, for example, it is well nigh impossible to squeeze the water out of it by any gross mechanical means.

Of the colloids that compose the mass of the animal body, the emulsion colloids constitute the chief bulk. In muscle, for example, we have about seventy-five per cent. water. Of the twenty-five per cent. of solids,

only one per cent. is ash; the rest is, in the main, emulsion colloid material.

Of the emulsion colloid material found in any cell or group of cells in the animal organism, the main bulk is protein, and, as this has been studied with special care by Hofmeister (34), Spiro (35), Pauli (36), Hardy (37), Wolfgang Ostwald (38), von Schroeder (39), Handovsky (40), Schorr (41), Gertrude Moore and myself (42), we will devote our chief discussion to it. In this way we shall get at once not only a simple explanation of many phenomena that are familiar to every worker in medicine, but valuable principles, upon which to base a rational therapy.

The proteins and the effect of various external conditions upon them have been studied from many points of view. Those which are most important from a medical standpoint are the relationship of water absorption to the state of the colloid, the viscosity of the colloid, and the precipitation or coagulation * of the colloid. As we shall see shortly, a very simple relationship exists between these apparently detached properties of the colloid. To indicate the importance of a knowledge of the changes that occur in these simple properties of the colloids under various external conditions, we need but mention the fact that the first of these properties of protein colloids controls, in the main, the whole question of how much water the cells or fluids of the body will hold under physiological and pathological conditions (normal cell turgor, 43; edema, 44); the viscosity of protein solutions is associated with the work the heart must do in pumping the blood, the general problem of protoplasmic motion (migration of leukocytes, contraction of muscle, 45), and the phenomena of cell division; their precipitation and coagulation, with such changes as the steaminess of the cornea in glaucoma (46), the graying of the parenchymatous organs in "cloudy swelling" (47), the changes produced by acids, caustics, and the metallic salts in pharmacology, etc.

It is convenient to begin our discussion with the matter of water absorption by such protein colloids as gelatin or fibrin.

When gelatin or some powdered fibrin is thrown into water it swells up somewhat (42). If the experiment is done quantitatively, and the gelatin or fibrin is thrown instead into a dilute acid, it is found that the colloid swells up very much more. Depending upon the concentration of the acid, these colloids swell more and more with every increase in the concentration. But this is true only within certain limits. After a time a point is reached where the gelatin or fibrin does not swell more

* It is necessary to distinguish between these two terms, for they represent radically different changes in the state of a colloid. We use the term precipitation if the change is reversible. We speak of the precipitation of a protein with a salt of some kind, if, on removing the salt, the protein goes back into solution. If it fails to go back into solution, we say it is coagulated—in other words, the change is irreversible.

with a further increase in the concentration of the acid, but less. While all acids make gelatin or fibrin swell, they are not equally powerful in this regard. When equinormal acids are compared, hydrochloric acid is found to act more powerfully than nitric, and this more powerfully than lactic or acetic, in the order named. Sulphuric acid stands below these organic acids.

These simple facts are of the greatest biological importance. What we have said regarding the action of acids on protein colloids can be said without modification for the effect of acids in the most varied physiological and pharmacological reactions. The same laws govern the way in which these acids reduce the irritability of nerves (26) and muscle (28), kill bacteria and the cells of higher plants (27, 30), affect the sense of taste (29), influence chemotaxis (Garrey, 32), favor the absorption of water by animal and plant tissues (42, 43, 44, 46), favor proteolysis under the influence of pepsin (48), etc. We are safe in believing, therefore, that the point of attack of the acids is the proteins in the tissues, and that they influence the various biological phenomena considered by changing the state of these colloids in the same way that they change the state of our gelatin or fibrin (49).

The swelling of gelatin or fibrin in any acid solution is markedly reduced through the presence of any salt, even a neutral salt (50). So, if we add sodium chlorid to a lactic acid solution, the gelatin or fibrin contained in this medium will not absorb as much water as when the salt is not present. The more salt we add, the more is the swelling of the colloid reduced, and if we add enough the swelling may be stopped entirely.

But the different salts are very unequally effective in this regard. If we compare a series of equimolecular salt solutions, say sodium salts, and at a concentration that we are likely to encounter under physiological or pharmacological conditions, it is found that these arrange themselves in a characteristic order. The chlorid, bromid, and nitrate reduce the swelling of gelatin or fibrin in an acid solution less than do the sulphocyanate, iodid, or acetate, and these less than the sulphate, phosphate, tartrate, or citrate. If, on the other hand, we compare a series of salts having a common acid, say a series of chlorids, the metallic elements in these salts assume a characteristic order. Ammonium, potassium, and sodium stand near each other; far more powerful than these are magnesium, calcium, barium, and strontium, and yet more powerful are copper and iron.

A similar series of statements may be made for the effects of different alkalies on the swelling of gelatin or fibrin, and for the effects of different salts in producing water absorption by these colloids in an alkaline medium.

When compared with the powerful effects of the electrolytes, the

non-electrolytes have but little effect in reducing the swelling of gelatin or fibrin in an acid solution. The amount of water absorbed by a given mass of gelatin or fibrin in a given concentration of acid is practically uninfluenced through the addition of urea, or ethyl or methyl alcohol. This is also true of glycerin, dextrose, saccharose, etc., in the lower concentrations, though in higher concentrations these inhibit the swelling of protein colloids in an acid medium. The same is true of the effect of non-electrolytes on the swelling of gelatin or fibrin in an alkaline medium. The reason why we lay stress upon the behavior in an acid medium is because we are chiefly interested in the carnivora, and the whole chemistry of these animals tends to run the reaction of their tissues over toward the acid side. Carbonic acid is the common product of normal carbohydrate and fat metabolism, and, when the normal metabolism gives way to an abnormal one, the tendency of the tissues to become acid is enormously heightened, for in place of carbonic acid much stronger acids are produced.

These facts may be at once transferred to our knowledge of the pharmacological behavior of many items in our pharmacopeia. We can see, first of all, why the electrolytes are in general far more active physiologically than the non-electrolytes. But we can go further than this. That long series of physiological reactions which we have found to be identical point for point with the reactions of these simple colloids toward various external conditions, may now safely be regarded as reactions on the part of the colloids of the cell toward these same external conditions.

A substance like fibrin, under ordinary circumstances, merely swells up in water; it constitutes a semisolid mass. The same is true of gelatin at lower temperatures. We can, without overstating the case, make the behavior of tiny fragments of fibrin identical with the behavior in certain directions of individual cells. Tiny fragments of fibrin have the consistency, the pliability, and the powers of water absorption and secretion that are possessed by the individual body cells, say, for example, the red blood-corpuscles. Fibrin behaves, therefore, like the solid constituents of our bodies. A mass of fibrin or a gelatin cake behaves not unlike a mass of animal cells. In certain directions a mass of gelatin behaves like a muscle, an eye, a kidney, or a brain. But such semisolid structures do not compose all of our bodies. Permeating these, we have streams of liquid colloid material called the blood and lymph, that are kept in constant motion by the heart, the pressure of muscles upon the vessels, the aspiration of the thorax, etc. We have been content to speak of these circulating streams thus far, in their relationship to the body cells, as identical with the pond water that washes about our primitive ameba. And this remains true, but there is one important difference between the pond water and our blood and lymph. This depends upon the fact that pond water is practically free from colloids; it is to all in-

tents and purposes plain water, in which some crystalloidal electrolytes and non-electrolytes are dissolved. Blood and lymph, on the other hand, are high in colloids. The water in pond water is essentially free. In the blood and lymph there is no free water; all the water is held in combination with the colloids found in them (10), and the electrolytes and non-electrolytes of the blood and lymph are carried in this colloid-water matrix (51).

The blood is essentially liquid in character. It corresponds in its behavior not with a solid cake of gelatin, but rather with a solution of gelatin; not with a mass of solid albumin like fibrin, but with a dissolved albumin like egg white, a globulin, or serum albumin. Let us ask, therefore, how such a solution of a protein colloid behaves under various external conditions. For an answer to this question we are especially indebted to Franz Hofmeister (34), Wolfgang Pauli (36), W. B. Hardy (37), P. von Schroeder (39), Hans Handovsky (40), and K. Schorr (41). When we deal with such liquid colloids we cannot use the characteristics that served us in a study of gelatin and fibrin. The absorption of water, for example, by a gelatin plate can be accurately followed by weighing the plate; in the case of fibrin we can measure the height to which weighed quantities of this substance rise in glass tubes of a standard diameter. In the case of a colloidal solution we may use changes in its viscosity, changes in its precipitability or coagulability under the influence of heat or various electrolytes and non-electrolytes, or changes in its optical behavior. While we shall learn later that all these are measures of the same type of change in the colloid, these properties are individually of such great biological and therapeutic importance that their individual discussion is not without value. A change in the viscosity of the blood (52) constitutes one of the great variables in the circulation, which determines how much work the heart must do to keep this fluid circulating; precipitability and coagulability of the liquid colloids of the body is associated with the production and absorption of corneal opacities, the changes incident to exposure of parts of the body to heat and cold, the phenomena of blood and lymph coagulation; the optical properties of a colloid solution are associated with the maintenance of the normal, and the establishment of abnormal indices of refraction in the clear media of the eye.

Wolfgang Pauli (53) has studied a very pure liquid albumin by working with blood serum from which the various admixed crystalloids have been removed through long dialysis of the blood against distilled water. Such a solution is perfectly clear and entirely stable. If the viscosity of such a preparation is measured, it is found to be considerably higher than that of pure water. If a trace of acid is added, the viscosity is enormously increased. But to this there is an upper limit. In the case of such acids as hydrochloric, hydrobromic, nitric, or sul-

phuric, a point is finally reached where a further increase in the concentration of the acid does not further increase, but decreases, the viscosity. For the weaker organic acids no such optimal point has yet been found.

The addition of any salt to an acidified albumin markedly reduces the viscosity. The addition of a non-electrolyte is conspicuously less effective in this regard. With the same salt the degree of reduction of the viscosity increases with every increase in the concentration of the added salt. With a given concentration of any series of salts very different effects are obtained. So, for example, when sodium salts are compared, the chlorid, nitrate, and sulphocyanate are found to be less powerful in reducing the viscosity of an acidified albumin solution than the acetate or sulphate.

A practically identical series of findings has been established for the effects of alkali and of alkali plus various electrolytes and non-electrolytes on liquid protein.

It is readily apparent from these remarks that the changes in the viscosity of a liquid protein and the absorption and secretion of water by gelatin or fibrin under identical conditions parallel each other. The fundamental change underlying both may, therefore, be looked upon as being the same. We shall call it a *change in the hydration capacity of protein colloids*. What makes our gelatin or fibrin swell increases the viscosity of serum albumin, and vice versâ. What increases the hydration of a colloid increases the intimacy of its relation to its solvent, and so the stability of the colloidal solution. It will not surprise us, therefore, to have it pointed out that those conditions which increase the hydration capacity of the protein colloids are the conditions which increase this stability, while conversely, those which decrease this must favor the precipitation and coagulation of the protein. A few illustrations of the behavior of protein toward various precipitants and coagulants will make this clearer.

The pure serum albumin already discussed is readily precipitated by heat or through the addition of alcohol. When a little acid is added to the blood serum the hydration capacity of the colloid is increased, and, corresponding therewith, its precipitability through heat or alcohol is lost. But if yet more acid is added the hydration optimum for the protein is exceeded, and now the heat and the alcohol again regain their power to precipitate the protein. In a similar way the protein that has lost its precipitability through heat, by having an acid added to it, has it restored when any salt is added, just as we previously found this to decrease its hydration capacity.

In this way we see how a series of reactions in certain protein colloids, which at first sight seem to have nothing to do with each other, all come to be reducible to a comparatively simple series of changes.

And so we also see how apparently widely separated and unrelated physiological, pathological, and pharmacological phenomena all come to be the expressions of the same simple underlying colloid truths. The mercury salt that kills bacteria, makes the tears flow and maybe blinds an eye; that kills in the same way some of the intestinal flora, produces a diarrhea and perhaps a coagulation necrosis of the mucous membrane, is only an electrolyte that is peculiarly powerful in making the hydrated protein colloids which we find in the body give up their water and suffer the optical and solubility changes that go with this process. And the changes that characterize a glaucoma, a nephritis, or a generalized edema are in the main only the expression of an increased hydration capacity of the tissue colloids involved, and can be relieved by using those same electrolytes which we found especially effective in decreasing the hydration of these same body proteins upon which any one may work in his laboratory.

THE EFFECT OF COLLOIDS UPON CRYSTALLOIDS

The previous paragraphs dealt in the main with the effect of various external conditions, notably various crystalloids, upon the state of the colloids that are of importance in the body. We wish now to briefly point out the fact that *colloids also affect the state of the crystalloids* that are brought in contact with them. So many problems in pathology and preventive medicine are associated with changes in the solubility characteristics of various substances found in our tissues and their secretions, that a brief reference to this problem is not out of the way (54). Not only is a normal or abnormal formation of bone a problem of this character, but so is the formation of concretions in the brain, in the gall-bladder, in the kidney or bladder, or the deposition of urates, etc., in the joints.

Wolfgang Pauli and M. Samec (55) have made a careful study of the solubility of various substances in colloidal protein solutions as compared with the solubility of these same substances in water. In general it may be said that the solubility of easily soluble electrolytes is slightly decreased through the presence of colloid material, while the solubility of difficultly soluble substances is, on the other hand, often very decidedly increased by this means. The removal or a change in the state of the colloid constituents of a body tissue or a body fluid, be this wrought through bacteria, a dietary régime, or a pharmacological preparation, may, therefore, be followed by consequences which, on the one hand, determine the relief of a rickets, the prevention of an attack of gout, or the prevention of the formation of a new set of kidney stones; on the other, by the hastening of an arteriosclerotic process, or the deposition of more urates, bile salts, or earthy phosphates in the form of stones.

SURVEY AND APPLICATION

We have laid special stress thus far upon the application of an isolated number of physicochemical conceptions to the individual cell. We have now to discuss these conceptions from the standpoint of groups of cells, for instance, as in such a multicellular organism as man. We will find that the same laws are operative here, but some have acquired an exaggerated importance, while others are hidden behind the complicating circumstances that spring out of the fact that the cells exist no longer individually, but in groups, and that special arrangements have been introduced to make life in such large groups possible. We no longer deal with the individual, but with the society made up of individuals, and, while the physiology of the whole is still only the compound physiology of the individuals, these individuals have so specialized in their work and have introduced such new schemes into their collective life, that this at first sight seems different from that of the individual who went to form the society. But it is not. A second fact that must have become apparent is that we have not been able to hold closely to our subject of therapy, but that we have found it necessary to move rapidly and easily between the realms of pure chemistry and physics and those of physiology, pathology, and pharmacology. The reasons for this are obvious. No real distinction exists between these realms. A therapy that involves discussion of so simple a matter as the rôle of sodium chlorid in the diet cannot be handled in any isolated way; we must know the rôle played by sodium chlorid and the theory of its action in normal physiology before we can intelligently discuss the effects of its elimination or its addition to the diet under physiological or pathological conditions.

Let us now see what use may be made of the principles discussed in the preceding pages when we deal with so complex an organism as man. We will begin with the rôle of water in our everyday therapeutic procedures, for, as we shall find, behind the biochemical behavior of water there is many a problem that at first sight appears to have nothing to do with this (56).

1. Rôle of Water

We ordinarily take the metabolism of water in the body largely for granted. According to his desires, the normal individual consumes per day several liters of water or liquids containing water, and after a comparatively short latent period he again eliminates this water in the form of urine, sweat, or through the breath. Water has gone into the body and come out again, and the body is to all intents and purposes unchanged. And this is why we are so likely to ignore entirely this most important function.

From these simple statements, let us remember first of all that we get a urinary output (or an output of water from the lungs or the skin, if the temperature is high) that is proportional to the amount of water consumed. The fact that the law of the conservation of matter and energy works for water as for any other substance introduced into the body is overlooked all too often in our daily practice. When we wish more urine (or sweat), we must give more water, and, other things being equal, we shall get this in proportion to the amount of water consumed. While a cry for more urine is heard daily in every hospital, the fact that we can obtain it only by giving more water to our patient is as constantly ignored. Only water will yield more urine. It is the one and only diuretic. The substances that we call diuretics are such only because they aid in supplying water, as we shall see shortly.

The loss of balance between the intake of water and the elimination of water from the body represents a pathological state. When water is retained in the body we call it edema. The opposite state is represented by an abnormal loss of water from the body, and is not so much discussed. Why has the normal body so constant a content of water, and what has happened when a patient has developed an edema or lost an abnormal amount of water? What principles must guide us in the treatment of the two last-named conditions?

The absorption and secretion of water by all cells and tissues that have been examined thus far have been found, point for point, to be identical, both from a qualitative and a quantitative viewpoint, with the absorption and secretion of water by such protein colloids as fibrin, gelatin, or serum albumin. Our ameba has a certain size under normal conditions in its pond water. This is identical with the amount of water absorbed by a flake of fibrin placed in ordinary water. If we add a little acid to the pond water, the ameba swells, or, if we add salt, it shrinks. This again is identical with the behavior of the fibrin flake in a dilute acid, or in a solution of salt.

A complex organism like a human being behaves in toto like the ameba. Under normal circumstances it has a certain water content which we cannot increase or decrease by the giving of water alone, any more than we can increase the amount of water held by the ameba by increasing the size of the pond in which he swims.

The human body is a system of colloids that is saturated with water, and mere water drinking, for example, will not increase the amount of water these colloids will take up.

How can we produce an edema? We can produce this only by increasing the capacity of the tissue colloids for water, so that when water is offered to them they will swell. The conditions that will thus increase the water capacity of colloids are various. In the case of the protein colloids we found that acids are particularly potent, and so are the various

proteolytic enzymes. Under the influence of an abnormal acid (or an accumulation of other substances that are capable of increasing the hydration capacity of the tissue colloids) we might, therefore, if a source of wafer is available, expect to have a water retention occur. The body colloids will swell; in other words, an edema will result. That such is the case has been proved by many experiments. Not only will injection of acid into an animal lead to the development of a generalized edema, but the various conditions that are known to lead to a water retention in the body are all such as have associated with them an abnormal production or accumulation of acid in the tissues, as, for example, heart disease, respiratory disease, blood-vessel disease, passive congestion, intoxication with anesthetics, intoxication with certain metals, intoxication with the toxins of many infectious diseases, etc. On the other hand, we have learned methods by which we can decrease the capacity of the tissue colloids for water. So, notably, we found that the various salts are active in this regard. We have normally a certain salt concentration in the body. If we increase it, the tissues give up water and the whole body loses weight, exactly as does our ameba when we drop him into a salt solution of a higher concentration than pond water. In the same way we lose water if hypertonic salt solutions are injected into our blood vessels, if we take a cathartic salt, or if we try to subsist on sea water.

An abnormally high or low water content may involve the whole body or it may involve predominantly only a single organ or set of organs. It may last a long time, as in elephantiasis; or only a short time, as in the loss of water following a cathartic. The abnormally high water content of various organs has, on the whole, the greater interest. This is the prominent sign in many a specially-named pathological condition. So, for example, in the edema that affects the eye (which we call glaucoma), in that which affects the kidney (which we call nephritis), in that which affects the parenchymatous organs (which we call cloudy swelling). The important point in all this, from a therapeutic basis, is that just as we can reduce the normal water content of cells and tissues by various salts, so can we reduce an abnormally high water content in these edematous states and by the same means. The saline cathartic that makes the normal body give up water will also make the edematous body or organ give up water, and here we have a rational explanation of the beneficent effects of the long established therapeutic use of these cathartic salts in edema. But the explanation of how they act has been lacking. We have been in the habit of saying that a cathartic salt makes for a secretion of water into the bowel, and so for a loss of water from the edematous tissues. It is more correct to say that the salts diffuse into the tissues, which then liberate water. This "free" water comes out either through the bowel or through the kidneys. And now we see, too, why the saline cathartics have so long been identical with the saline

diuretics. They act on the tissues with which they come directly in contact (bowel and kidney), and they also act on all the other tissues of the body, an action quite as important as that on the bowel and kidney alone, for only in this way is "free" water rendered available for elimination by these secretory organs (see below).

Not alone have we learned in this way what is best in the therapy that the past has taught us, but we have also learned to become critical of other therapeutic measures that have thus come to us.

So, for example, we must feel it wrong to stop the intake of water by an edematous individual in the hope of decreasing his edema, or to stop it in a case of acute nephritis because we think this will throw work on the kidneys, when we wish to "spare" them. The giving of water can only indirectly aggravate an edema. A swelling kidney or brain tends to shut off its own blood supply and so to add to the conditions which are increasing the hydration capacity of the involved tissues. We meet the danger incident to giving pure water (which allows the colloids to swell) by giving along with it certain salts. An edema is a self-limiting affair; the involved organ will take up water only to the saturation point of its colloids. And not until these colloids are saturated will any "free" water be left over to become available for urine. If we withhold water in order to reduce an edema, we may at the same time expect no urine and no sweat. Instead of increasing an edema, water is, in the aggregate, more likely to decrease it. In being eliminated, the water carries off with it the substances which increase the hydration capacity of the tissue colloids, thus decreasing this hydration capacity and consequently the edema.

The electrolytes all decrease the capacity of the tissue colloids for water. As sodium chlorid is one of these, we shall be unable to subscribe to the idea that a restriction of this salt in the diet is right when we are trying to reduce the edema in a patient. Sodium chlorid should, on the contrary, be urged upon the patient in his food, between meals, and, if necessary, it should be given him by rectum or intravenously.

Whether we deal with a generalized edema or with a local one, the principles underlying its relief are always the same. Therefore we shall not be surprised to find that, just as sodium citrate will make the intestinal mucous membrane give up water, it will also, when injected subconjunctivally, make a glaucomatous eye give up water, so relieving the glaucoma. Or, if a kidney has ceased to functionate because of a pregnancy intoxication or the action of an anesthetic or the toxin of an acute infectious disease, this may usually be relieved by injecting sodium chlorid (and sodium carbonate to neutralize acid) intravenously in hypertonic solution. This makes the kidney colloids shrink, and the decrease of swelling allows the kidney to get a normal blood supply once more. By acting upon the edematous brain, the edematous optic nerves,

and the body tissues generally it reduces the headache, vomiting, blindness, and the edema of the body tissues generally. At the same time the water freed in this way becomes available for urine, and the urinary output rises.

In this connection it is well to emphasize two more points. The first of these is the reciprocal relationship that exists between the various secreting organs of the body. Since the *sine qua non* of every secretion is the obtaining of free water, it is clear that, if we use this up for one secretion, we cannot have it for another—a point that is frequently lost sight of. If we wish to have urine from a kidney we cannot expect it if we are robbing the body of all its free water by sweating our patient (unless we cover this by giving water); or, if we are robbing the body of water through a secretion into the bowel, we cannot at the same time have the water for urinary output or sweat.

If these physicochemical conceptions are correct, then we have also an insight into the "diuretic" action of various pharmacological products. The caffein derivatives and digitalis will serve as good examples. We have already emphasized the fact that only "free" water goes to the formation of any secretion. These "diuretics" can act, therefore, only because they furnish free water. This they do by increasing the force or the frequency of the heart beat and the depth and rapidity of respiration. In this way there is kept in contact with the body tissues a blood higher in oxygen and lower in carbonic acid than is the case when these drugs have not been taken. By this means the normal (or abnormal) acid content of the tissues is reduced, in consequence of which the hydration capacity of the tissue colloids is decreased. "Free" water is then given off to the blood, which may then escape as urine (or as some other secretion).

Conversely, we may expect a drop in all the secretions and a retention of water if we give any drug that has an opposite effect. The anesthetics, alcohol in large amounts, atropin, morphin, etc., are examples of this class. These all permit a greater than normal accumulation of carbonic (and other) acid in the tissues, and correspondingly they will decrease the output of urine, create thirst, lead to constipation, check sweating, etc. At the same time we learn from these simple facts that a reciprocal relation exists between the matter of water absorption and water secretion—the one is a mirror of the other, and that which favors the one at the same time hinders the other.

What we have said holds for the ill as for the well body. In concluding these paragraphs it is only necessary to point out that, while in the ameba we deal with a mass of colloid material so small that secretion or absorption affects the whole, this does not follow in the case of so large a colloidal mass as the human being. Here one organ or set of organs may be busily absorbing water, while another is

equally busy giving it up. A few words regarding this are of therapeutic interest.

The problem involved is clearly presented to us under physiological conditions in that almost any amount of water we choose to consume is absorbed from our intestinal tract, while an equal amount (skin and lungs ignored) is given off by the kidneys. What is the mechanism that accomplishes this?

Let us first ask what happens to the swallowed water, and how it goes to form urine. What have these problems to do with our ameba swimming about in its pond?

We have already paralleled the general processes of water absorption and water secretion in the ameba with the behavior of a fibrin flake under similar conditions. The ameba is a spherical mass of colloidal material that is saturated with water, and, through changes in its physicochemical surroundings, or through direct changes in its own chemical composition, it at times takes up water (absorption), at times gives up water (secretion). But in a multicellular organism the phenomena of water absorption and secretion that confront us do not at first sight seem to be interpretable on any such simple basis as that outlined for the ameba. In man, for example, we find whole organs set apart, and seemingly endowed only with powers of absorption, while others are apparently set apart to functionate only as secretory organs. It becomes hard, for example, to see just what relationship exists between a mucosal cell of the small intestine, concerned almost exclusively with an absorption of water from the lumen of the gut, or a kidney cell, concerned equally exclusively with a secretion of urine, and the ameba which now absorbs and now secretes water either in response to its own physiological demands or under the conditions with which experimentally we are pleased to surround it. And yet on closer analysis the difference between the two is not so striking.

First of all, we appreciate the fact that the mucosal cell is an absorbing cell only so long as we look at it from the side of the lumen of the gut. If we regard it from the blood vessel side, it is a secreting cell, for what it absorbs from the gut it gives up to the blood. Similarly, the kidney cell is a secreting cell only because we usually look at it from the point of view of being a producer of urine; as a matter of fact, everything that goes to make up the normal urine was absorbed from the blood. But, even if we look at the matter from the narrower point of view, the intestinal cells under certain circumstances become secreting cells, in that they secrete substances into the lumen of the intestines, and, according to judgment of some authors, certain kidney cells may reabsorb materials that have been secreted by others. In essence, therefore, secretion and absorption in the higher animals is not different from absorption and secretion as observed in an ameba. That which

remains, therefore, to characterize absorption and secretion in the higher animals is merely this: that, under normal circumstances and from the point of view of the organism as a whole, absorption and secretion occur predominantly in one direction. What require special analysis are the conditions existing in the multicellular organism which make it possible for certain cells and tissues thus to act predominantly as absorbing systems, while others act predominantly as secreting systems.

Let us see if we cannot define in general terms what must be the conditions lying at the bottom of this predominant functioning of certain cells and tissues in one direction, and do so on the basis of our belief that the colloidal constitution of the living cell is primarily responsible for the phenomena of water absorption and secretion by the cell.

The ameba, or an isolated cell or tissue derived from a higher animal, kept in a solution of any kind, is surrounded by this solution on all sides. Could we imagine the chemical processes within these cells held in abeyance, then we can see how these cells would after a time get into a state of equilibrium with their surroundings. When this is brought about the cells neither absorb nor secrete water. Only as this equilibrium is disturbed, either through changes in the surroundings of these cells or through the specific chemical changes occurring in the cells, can we expect a renewed absorption or secretion.

Under quite different conditions do we find the individual cells of the multicellular organism existing in the intact living body. While in a certain sense the internal activities of the ameba may be compared with those of the individual cells making up, say, the intestinal mucosa, and there exists a certain analogy between the fact that both are surrounded by a liquid medium, with this the analogy stops. For, while the ameba is surrounded on all sides by the same liquid medium, the cells of any of the absorptive or secretory organs found, for instance, in a mammal, are, with different parts of their cell protoplasm, in contact with entirely different media. The cells constituting the intestinal mucous membrane are bathed on the one side by intestinal contents, while on the other they are bathed by blood or lymph, or both together. Such cells, like any other absorptive or secretory cells similarly situated, are, therefore, in the predicament of trying to get into equilibrium with as many different media as surround them. It is in trying to do this that all the phenomena which we call absorption and secretion in the higher animals are produced. It is during its attempt to get into equilibrium with the intestinal contents on the one side and the blood on the other that the mucosal cell (better, the colloidal membrane separating the intestinal contents from the blood) absorbs the intestinal contents and transfers them to the blood.

The body of a multicellular organism, such as a mammal, is like the individual ameba built up of colloidal material, which in the resting

state is saturated with water. To be counted in with the colloidal structures that make up this water-saturated colloidal system of the mammal, and composing an integral part thereof, are the blood and the lymph. The entire system will not take up more water, nor give up any, except as chemical changes are first produced in it which either increase or decrease the capacity of the tissue colloids for water.

The relationship between the absorption of water from the intestinal tract and its secretion subsequently by the kidney is easily understood when the following is borne in mind. The cells of the small or large intestine will absorb water only if they are not already saturated with water. In consequence of the carbonic acid production in these cells, they are rendered capable of taking up water from the intestinal lumen. But, as the blood circulates through the intestinal mucous membrane, the carbonic acid diffuses over into it. Two changes follow this: First, the capacity of the colloids in the mucous membrane to hold water is diminished; and, secondly, the capacity of the blood (which we have said represented a water-saturated colloidal solution) to take up water is at the same time increased. A minimal calculation shows that a liter of blood in passing through the intestinal tract, where it changes from arterial to venous blood, is made capable in this way of taking up at least 17.5 cubic centimeters of water. As long as the circulation is maintained, and as long as the cells produce carbonic acid, the intestinal tract must, therefore, absorb water, if this is made available by being in the lumen of the gut. Evidently the higher the carbonic acid (or other acid) content of the blood, the better absorbing medium for water must it become. And so we are not surprised to note that water is best absorbed from the large bowel where the blood has a most highly venous character, and less well from the small intestine, where this is not so markedly true. Water absorption from the stomach is scarcely possible, for this is so richly supplied with arterial blood that its acid content scarcely varies.

Just the reverse conditions are necessary if we are to obtain a secretion of water. A secretion can be gotten only from arterial blood, that is to say, blood low in carbonic (or other) acid. The venous blood, which has grown rich in carbonic acid and water in its passage through the intestine, loses the carbonic acid (as CO_2) when it passes into the lungs. When this happens the colloids of the blood can no longer hold all the water they had absorbed, so it becomes "free." This arterial blood with its "free" water passes to the kidney, and here the free water is eliminated as urine.

We are not surprised on this basis to find that during absolute starvation the secretion of urine ceases (practically) entirely. If the colloids of the body as a whole are saturated with water, none is left over to be secreted. Only as the tissues undergo a gradual consumption during

starvation, or their colloids suffer changes which decrease their capacity for holding water, is any liberated to become available for secretion.

On the other hand, as we have already pointed out, if an animal that has its body colloids saturated with water consumes a quantity of water, after a time an amount of urine (or sweat or breath moisture) is secreted which is equivalent to the amount that has been drunk. It does not matter how this water was introduced into the organism. It may have been swallowed or introduced through a stomach tube into the gastrointestinal tract, or it may have been injected into the peritoneal cavity, under the skin, or directly into the blood. But let it be noted that the diuresis occurs only in proportion to the amount of "free" water present; in other words, as water not combined with a colloid.

The correctness of these ideas is at once proved when we make the experiment of injecting intravenously in place of a physiological salt solution an equal volume of a solution in which the water is not "free," but combined with a colloid (that is, in the form in which it exists in the body cells and fluids normally). Under such circumstances no increased water secretion in the form of urine (or sweat) results. When blood or blood serum or a gelatin solution is injected intravenously, no increased urinary output follows.

These facts are of considerable therapeutic worth. We have emphasized the fact that, if we would get any urine (or sweat) from a patient we must first have all his tissue colloids saturated with water. After this has been accomplished, we shall obtain from him a urinary (or sweat) output only as we have administered water over and above the amount necessary for the saturation of all his colloids. Then we shall have a urinary output that is in proportion to the amount thus introduced. The blood is not that fathomless well for urine that many clinicians imagine it to be.

Let us ask now what happens, so far as urinary secretion is concerned, if we introduce with a given quantity of "free" water varying amounts of any salt. In discussing the absorption of water by protein colloids we found that all salts decrease the capacity of these colloids for holding water. We are not surprised, therefore, to note that if we inject progressively stronger sodium chlorid solutions intravenously we get (with a constant amount of water injection) a corresponding increase of urine. It is ordinarily said that such salt solutions "stimulate" the kidney. Aside from the fact that the word *stimulation* means nothing, this is too narrow an interpretation of the case. As we give progressively stronger salt solutions, we increase more and more the concentration of salt in the body tissues, which then give up water. This water is "free" and adds itself to the free water that we have introduced; therefore, we have a greater amount available for secretion as urine, sweat, etc.

While sodium chlorid makes a protein colloid give up water, other

salts, like sodium phosphate, sodium sulphate, sodium citrate, magnesium sulphate, magnesium citrate, etc., act far more powerfully in this direction. It is because of this more powerful action that they are called the saline diuretics. Their behavior is to be explained in the same way as the behavior of sodium chlorid—they make the tissues of the body yield up water.

The list of these saline diuretics is identical with the list of the saline cathartics. The reason for this is obvious. The saline cathartics do to the gastrointestinal tract what they do to any protein colloid, as F. Hofmeister (57) first showed. In spite of the many complex explanations of the action of the cathartic salts that have been advanced since Hofmeister's work, we are destined to accept his explanation (58).

We have now to look at our problem from another point of view. While sometimes we desire the body colloids to give up water, nature at times furnishes pathological conditions in which we desire just a reverse result.

We can illustrate what is meant by referring to the problems presented by such conditions as hemorrhage and shock (59). The two conditions are mentioned in the same sentence not alone because, from a clinical standpoint, they have much in common, but because this is also true from a therapeutic standpoint. In both we have a diminution in the volume of the circulating blood, and a good part of the therapy of these conditions consists in combating this sign by attempting to increase the volume of the circulating blood. The various therapeutic schemes that have been devised to accomplish this end are familiar to everyone. What are their relative merits (60)?

It is at once apparent that the injection of salt solutions into such individuals can yield only temporary results. We inject free water in this way, and free water does not remain in the blood vessels, but escapes in a short time through the various secretory organs of the body, or is sucked into the tissues which, in hemorrhage or shock, are likely to have an increased capacity for water. Only water in combination with a colloid will and can remain in the blood vessels, and hence the better results to be obtained by introducing, instead of salt solutions, blood, blood serum, or, if necessary, gelatin solutions.

The same problem confronts us in the treatment of such a condition as constipation when due, as is so often the case, to a too perfect absorption of water from the intestinal contents. When we do not wish to prevent so perfect an absorption of water from the intestinal tract by giving cathartics which tend to make for a secretion of water into the bowel, then we can regulate the process by feeding material from which the intestinal mucous membrane cannot absorb the water. It cannot do this if we keep the water in the intestinal contents bound to a colloid. That is what happens when we prescribe a diet rich in cellulose, or add

to the ordinary diet such substances as agar-agar (61), or the various Japanese sea-weeds from which this is made. Cellulose and agar-agar are colloidal substances that have a great affinity for water, so they hold it in the gastrointestinal tract in spite of the efforts of the colloids of the intestinal mucous membrane to get it out. Because these colloids cannot get this water out, the intestinal contents remain soft, and so constipation is prevented.

2. Absorption and Secretion of Dissolved Substances

We have purposely laid so much stress upon the question of water absorption and water secretion from the body because *the absorption and secretion of dissolved substances* are intimately associated with and largely dependent upon this (56). Not only does this hold for the normal absorption and secretion of such substances as serve as foods or represent metabolic waste products, but also it holds for the absorption and secretion of substances which, either from a quantitative or a qualitative standpoint, are known to us as parts of our pharmacological or therapeutic armamentarium. The general problems of *intoxication and detoxication* are found here (62).

Let us first look at the problem as a whole.

We have in the earlier parts of this chapter always emphasized the behavior of the individual cell. The reason for this lies in the fact that the multicellular organism and its behavior represents merely the compounding of the behavior of many such cells and different kinds of cells. So we shall not be surprised to find that everything we have said regarding the unicellular organism holds for the multicellular one, except that in this certain additional factors are introduced which somewhat complicate the picture and demand separate analysis.

But just as we were able in a rough way to look upon man, for example, as a huge mass of colloidal material which collectively resembled the small mass represented by an ameba in its behavior toward water, so similarly can we compare the large mass with the small in its behavior toward dissolved substances. The ameba obtains all the various substances that it takes up from those which are dissolved in the water surrounding it; and it rids itself of such dissolved substances as it may have in excess in its protoplasm to this same water surrounding it.

A human being does in toto the same thing, only the mass of water available for such purposes seems comparatively small, and the processes of absorption and secretion of dissolved substances seem to be more intimately associated with certain organs. Thus we usually absorb a food or a toxic agent from an aqueous solution of this contained in the gastrointestinal tract; we rid ourselves of these same substances by

giving off an aqueous solution of them that we call urine. But the processes involved in these apparently complex acts are in essence no different from those which we encountered in our ameba.

All the absorbing and secreting systems that we encounter in the human body may be roughly divided into three phases. In the case of such an absorbing system as that presented by the intestine, these are represented by (*a*) the material to be absorbed, (*b*) the absorbing tissue, and (*c*) the blood or lymph. In the case of a secreting system, such as is represented by the kidney, we similarly recognize three phases: (*a*) the blood or lymph; (*b*) the secreting tissues; (*c*) the urine.

Let us take up first the matter of absorption and see what the general mechanism of this is in the case of the human being.

When we take a meal or swallow a drug it is practically equivalent to saying that we take an aqueous solution of something. This aqueous solution may contain colloids (such as our ordinary foods, the starches, proteins, and fats), or crystalloids (such as salt, cane sugar, strychnin hydrochlorid, or Fowler's solution). This is the first phase of our absorbing system.

The second is a colloid membrane that is made up of all the structures lying between the solution of substances to be absorbed and the blood or lymph. This colloid membrane is, therefore, a fairly firm structure, like a water-soaked leaf of gelatin. Only it may not be so entirely homogeneous. For instance, we recognize the differences that may result from having different kinds of cells in this absorbing membrane, and then between the different cells there may lie intercellular substances that need not be identical with the material that builds up any or all the various cells found here. But for the sake of simplifying our argument let us imagine it to be entirely homogeneous.

The third phase in our absorptive system is represented by the blood. This is also made up of colloidal material, but it is not solid, it is liquid. It corresponds, therefore, to a solution of gelatin.

What must happen in such a system?

We have already discussed what must happen so far as the water contained in the first of these systems—that is, the water in the lumen of the gastrointestinal tract—is concerned. The next fact to be emphasized is that the absorption of this and the absorption of substances dissolved in it are two distinct processes. *A solution is never absorbed as such.*

Let us here interject that the mixture which we originally introduced into the gastrointestinal tract undergoes a simplification to this extent: all the various colloids that may have originally been in it are converted into crystalloids before they are absorbed. From an academic standpoint this is not strictly true, but for practical purposes it is. The colloidal proteins are converted into aminoacids; the colloidal carbohydrates into

dextrose; the colloidal fats into fatty acid and glycerol; colloidal drugs are converted into crystalloidal form, etc.

Whenever a solution is seen to be absorbed we are observing the composite of the absorption of the solvent plus the absorption of each individual substance dissolved in that solvent. For example, when any solution is introduced into the intestine, each one of the dissolved substances diffuses into the wall of the intestine until an equilibrium is established in the distribution of each of these substances between the liquid phase represented by the solution and the more solid phase represented by the (colloidal) intestinal wall. Similarly, every substance present in the intestinal wall tends to diffuse out into the solution to the establishment of an equilibrium. In biological material it has been very generally assumed that the distribution of dissolved substances between two such phases attains an equilibrium when the concentration of any dissolved substance is the same in both. Such an *a priori* conclusion is entirely unjustified. We deal in this problem with the distribution of a dissolved substance between water and a colloid, and, as we know from the facts now available on this subject, equilibrium may be reached when the dissolved substance is contained in less, the same, or a higher concentration in the colloid than in the solution surrounding it.

Now, while the absorptive membrane is trying to get into equilibrium with the solution to be absorbed on the one side, it is also trying to get into equilibrium with the blood on the other. The problem of the "selective" absorption of the dissolved substance is the problem of the agencies concerned in establishing an equilibrium between all the various dissolved substances in these three phases. As we pointed out above, the factors of greatest importance in such a problem are the character of the various colloids concerned and their physicochemical state, as determined through the presence of acids, alkalies, salts, and various non-electrolytes; the nature of the dissolved substances to be absorbed and their rate of diffusion; the presence or absence of lipoids in the colloidal absorbing membrane and in the blood, etc. In other words, the laws of adsorption, of partition, and of chemical combination are all at work. Therefore, to the process of simple diffusion in this matter of absorption (or secretion) become added a number of secondary phenomena that obscure its purity. But this does not make questionable the fundamental importance of diffusion itself in the processes of both absorption and secretion.

To illustrate, let us try to follow the relatively simple process of the absorption of a strong (so-called hypertonic) sodium chlorid solution introduced into the intestinal tract (or into the peritoneal cavity, or under the skin). Both the water and the salt immediately begin to diffuse into the absorbing membrane. As diffusion progresses, the concentration of the sodium chlorid in the absorbing membrane rises. This rise in

concentration so affects the colloids of the absorbing membrane that they stop taking up water, or, if it becomes sufficiently high, an actual secretion of water into the gut or peritoneum or subcutaneous tissues results. While this is occurring, an equilibrium is tending to be established between the sodium chlorid in the solution undergoing absorption and the salt in the absorbing membrane, but is never attained under normal circumstances, because the salt in the absorbing membrane is at the same time trying to get into equilibrium with the sodium chlorid in the blood. Now, since the blood is circulating, it is evident that the equilibrium is constantly being broken down toward the side of the blood. In consequence of this, more and more salt must move over into the blood (be absorbed). But, as this goes on, the colloids of the absorbing membrane again return to a more "normal" state, and so the absorption of water, which could not occur before, can again take place.

With a dilute (a hypotonic) solution of sodium chlorid, the water does not meet with so great a resistance to absorption, and it is possible for such a solution to become more and more concentrated as the water is (the more rapidly of the two) absorbed from it. Even salt solutions isotonic with the blood must be absorbed. We were never able to explain this on our old osmotic conceptions of water absorption, because no osmotic differences exist in such a case to make the water move, but on the colloidal basis there is no difficulty in interpreting what happens. Let the colloids of the absorbing membrane take a little water from the isotonic solution and salt must quickly follow, for now its concentration is no longer in equilibrium with the sodium chlorid in the absorbing colloidal membrane. As the water passes over into the blood more water goes into the absorbing membrane, and then more salt, until all is absorbed. Or we can start the absorption by having a little salt go in first, and then the water, etc., for, if the truth be told, we do not yet know just what characterizes the "isotonic" solution, nor shall we until the colloidal constitution of living matter has been adequately taken into account.

As a final word let it be added that, on the basis of these colloidal conceptions of absorption, we experience no difficulty in understanding why any solution remaining for longer periods in the intestine or in the peritoneal cavity may, while it is being "absorbed," have appear in it various substances found in the blood or tissues which it did not originally contain. As dissolved substances diffuse out of a solution undergoing absorption into the absorbing membrane until an equilibrium is established, just so, of course, must the substances contained in the absorbing membrane tend to diffuse into the solution.

The fact will, therefore, not surprise us that, when a mixture of different dissolved substances is offered the intestinal mucous membrane for absorption, these substances are not all absorbed at the same rate or

in the same relative proportions. Neither are we surprised that the absorption is "selective." We should be more surprised if it were not. The selective character of absorption depends upon the fact that the absorption of water and the absorption of dissolved substances are separate processes. Of the dissolved substances each moves at its own rate and is influenced in its movement by factors that may not affect the others in the same way nor to the same degree.

The mechanism of the *secretion* of dissolved substances is the mirrored reflection of what has been said, and may be best outlined by discussing the secretion of dissolved substances from such an organ as the kidney.

What has been most difficult to explain in secretion has been its selective character; in other words, the ability of the kidney to separate from the blood a liquid which has a totally different quantitative and qualitative composition. Qualitative differences are for the most part explainable through chemical changes that occur in the secretory cells themselves whereby substances are produced (such as mucin, for example) which do not appear in the blood at all. In other respects a secretion differs only in quantitative composition from the blood. This may go to the point of having entirely absent from a secretion certain constituents of the blood, as, for example, albumin from the normal urine. For the most part, however, the secretion contains some substances in higher, others in lower, concentration than the blood. To limit ourselves again to the urine, we need by way of illustration only recall that, under ordinary circumstances, the urine contains less chlorid than the blood, and more sulphates and urea. How are such differences to be explained?

To begin with, it is well to call to mind that a secretion of dissolved substances is possible only so long as water is furnished the living organism. A secretion of water is necessary before we can hope to have any secretion of dissolved substances. This is a physiological truth that is utilized daily by the intelligent physician when he orders the drinking of large amounts of water to aid the organism in ridding itself of any poison, as the toxin of an infectious disease, for example. How the secretion of water by the kidney may be made a continuous affair we have learned from our previous discussion. How it must make for a continuous secretion of dissolved substance is apparent from what follows.

Let us recall here our division of the urinary secretory system into its three parts: the blood, the secreting membrane, and the urine; and our brief characterization of the first as a liquid colloid in which various crystalloids are dissolved, of the second as a solid colloid also containing various crystalloids, and of the third as a watery solution of various crystalloids (practically) free from colloids. Thus far our discussion has shown that under the conditions normally existing in the body no water can be introduced into the blood without getting the secretion of

an equal amount as urine (63). And what is secreted as urine is water, and only secondarily do substances come to be dissolved in it, so that it assumes a chemical composition which permits it to be characterized as urine. Let us see now what must happen if some soluble (or pseudo-soluble) substance is introduced into the blood. To simplify the problem and not make our discussion unnecessarily long, let us think of the blood as one homogeneous system, and the urinary membrane as another. Under such circumstances one of three possibilities presents itself from a physicochemical standpoint. The dissolved substance may distribute itself uniformly throughout the blood and the urinary membrane, or it may be present in either a greater or a less concentration in the urinary membrane than in the blood. Just what will happen is dependent upon the nature of the dissolved substance and the physical and chemical composition of the blood and the urinary membrane at the time. Of greatest importance are such facts as the presence and absence of lipoids, the character of the colloids concerned, and the state of these colloids as determined by the presence of acids, alkalies, salts, or various non-electrolytes. In other words, the laws of partition and the laws of adsorption again come into play. These differences in the distribution of a dissolved substance between the blood and the urinary membrane are rendered strikingly apparent when dyes are used as the dissolved substances.

But this distribution of a dissolved substance between the blood and the urinary membrane represents in the end only a *static* affair, and the secretion of dissolved substances in urine is a *dynamic* one. It requires no special comment to see now why only through the continuous secretion of water from the kidney can a continuous separation of dissolved substance from the urinary membrane (secretion) be rendered possible. The presence of water in Bowman's capsule and in the uriniferous tubules introduces the third phase into our secretory system and continuously breaks down the equilibrium that is trying to become established between the dissolved substance in the blood and the dissolved substance in the urinary membrane.

The attempt to establish an equilibrium between the dissolved substances in the urinary membrane and the dissolved substances in the urine (originally only water) as it passes down the uriniferous tubules, makes for a diffusion of dissolved substances out of the urinary membrane. Consequently as long as water is being secreted by the kidney this must tend to destroy the equilibrium which is trying to become established between the dissolved substances in the blood and the dissolved substances in the urinary membrane. If we recall the physicochemical fact that, when any dissolved substance is offered simultaneously a liquid colloid, a solid colloid, and water (as is the case in the kidney), an unequal distribution of the dissolved substance among the three phases is the rule, then we

shall have no difficulty in understanding why a difference in quantitative composition between the blood, kidney tissue, and urine, so far as dissolved substances are concerned, is also the rule. Therefore, a "selective" secretion is to be expected rather than to be wondered at.

Further than this we cannot pursue this subject at present. But in passing I should like to point out that the fruits of colloid chemistry help us to understand even the most radical differences that exist between secretions and their source. None is perhaps more striking than the strongly acid reaction of the urine or the gastric juice against the practically neutral reaction of its source, the blood. But even these can be accounted for through the selective absorption by the colloids of the urinary membrane of the sodium dihydrogen phosphate, and by the colloids of the gastric mucosa of the hydrochloric acid of the blood. Such a concentration of an acid by colloids from very dilute solutions of acid salts or acids has been proved directly (64).

What we have said concerning the absorption of dissolved substances in the intestinal tract and the secretion of dissolved substances by the kidney, may be applied with small variation to any other absorptive or secretory system that we find existing in the body. It may be applied also to any of the processes of absorption and secretion as these involve any cell, group of cells, or organ outside of those included in any special discussion of absorption and secretion. When we deal with such an organ as the brain, the spleen, or the adrenal, the system involved is really somewhat simpler than in the case of the intestine or the kidney. The individual cells of these organs are more like the ameba in its pond water—they are more nearly surrounded on all sides by the same fluid medium, and from this medium (the blood or blood plasma which we call lymph) they absorb the substances necessary for their existence or harmful to it, and, similarly, they give off to this medium their normal metabolic products or the substances which as toxic bodies may have gotten into them. The whole problem, therefore, becomes in the main a distribution of dissolved substances between (roughly) two media, on the one hand the cells and their intercellular substances, on the other the blood (or lymph).

The various normal and abnormal dissolved substances come to all the cells in the body through the same blood stream. The cells endeavor to get into equilibrium with each one of these substances. But, as the individual cells of the body differ from each other in chemical composition, or as the same cell is in a different physicochemical state at different times and under different conditions, so will the different cells, or the same cell at different times, behave entirely differently toward the same dissolved substance or substances as these are brought to them in the blood (65). It is for this reason that, not only the rate at which any dissolved substance is taken up will be different for different cells

or the same cell under different conditions, but the absolute amounts taken up will also vary.

From this we may understand why, although one blood bathes all the body tissues, one tissue is high in potassium while another is low, and while one takes up much calcium another refuses it almost entirely. It is for this reason that the spinal cord takes up relatively more strychnin than any other tissue in the body, that anesthetics go into the central nervous system, that tetanus toxin picks out chiefly the peripheral nerves, that when any "vital" stain is introduced into the body only certain tissues are deeply stained, that when salvarsan is given intravenously it is taken up chiefly by the (cells of the) spirochetes, and to their destruction. A specific poison, like a specific cure, becomes known to us whenever we discover some substance which, when offered the healthy or diseased human body, distributes itself in such a way between the various (colloidal) phases that make up the human body as to appear in a toxic concentration in the cell or organ under consideration before it does this in any other or all the other cells or organs of the body.

It is well here to emphasize again the fact that intoxication at all times depends upon the *concentration* of the toxic substance present, and not upon the absolute amount given. The whole principle of detoxication depends upon the recognition and use of this fact. We can easily illustrate what we mean when we discuss the intoxication that goes with any acute infection. Here we have an organism producing a poison at a fairly uniform rate. Where we do not possess a specific therapy much of the art and science of treatment consists in keeping the concentration of this toxic substance as low as possible. How do we manage this? When we cannot influence the factor of toxin production, we have only one way at our disposal, and that is to keep the concentration of the toxins as low as possible. To do this we can do but one thing, namely, give water.

As we noted above, the giving of water makes for a secretion of water, and this secretion of water is necessary before we can get a secretion (washing out, 62) of any toxic substance. By washing the toxic substances out of the kidney cells, for example, we break down the equilibrium existing between the toxic substance here and that in the blood. So more toxic substance will move from the blood over into the kidney to be eliminated *if the third phase is created by giving water.* But when the toxic concentration in the blood falls, the toxins from the cells will move over into the blood, and the lower we can keep the toxic concentration in the cells the less the intoxication and consequent pathological effect upon them. Now we also see the sense of giving water not only in a haphazard way as the patient may desire it, but in specified doses at regular intervals day *and night.* Otherwise during the periods of water abstention the toxin concentration will run up. What happens is

illustrated by the variation in the concentration of the normal constituents eliminated in the urine in any twenty-four hours. Since we are accustomed to consume most water with our meals, the urine after our meals is pale and low in urinary constituents. It is deep-colored and highly concentrated on rising in the morning, for through the night we do not consume any water.

OSMOSIS AND THE QUESTION OF CELLULAR "MEMBRANES"

In our analysis in physicochemical terms of certain phenomena familiar to every worker in the art and practice of medicine, we have almost ignored the much-discussed question of osmotic pressure. We have not done this unthinkingly, but because we feel that all those phenomena which are usually discussed under the heading of the osmotic phenomena of cells can more easily and more satisfactorily be explained on the basis of the colloidal constitution of living matter; and because we feel that the great mass of facts which has stood against the general applicability of the laws of osmotic pressure to cells can also be better explained on the colloidal basis. We see no reason, therefore, for calling upon a complicated osmotic system for further help (66). But this point of view is not yet generally accepted in the biological sciences, and so we wish to summarize briefly some of the experimental and theoretical evidence usually adduced in favor of the osmotic conceptions of the absorption of water and dissolved substances in the body, examine it critically, and then briefly indicate how this may be used to better advantage in support of our colloidal conceptions of absorption.

The widely divergent and contradictory "osmotic" conceptions of absorption and secretion as upheld by different workers at the present time had their beginning in the original osmotic investigations of DeVries and Pfeffer. In order to account for the "turgor" (that is, water content) of plant cells, these authors held that the individual cells were surrounded by "osmotic" "membranes" of such a character that, while they allowed water to pass through them, they did not permit substances dissolved in this water to pass through. On this basis they explained the observation that plant cells swell up in water low in dissolved substances, and shrink in more concentrated solutions, by saying that in the former case water is sucked into the cell, while in the latter it is sucked out. The movement of water into and out of the cell occurs until the (osmotic) concentration of dissolved substance is the same on both sides of the membrane postulated to exist about the cells. But, in order to permit the water to move, this membrane must be impermeable to dissolved substances (otherwise, of course, the dissolved substances would simply move from a region of higher concentration to one of lower concentration, and

so osmotic differences could not come to pass, and consequently there would be no movement of water).

From these observations and theoretical views sprang the interest of the physical chemists in the whole problem of osmosis and so we see constructed the various "osmotic cells" that may be seen in any physicochemical laboratory. Pfeffer was again pioneer here. He conceived the idea of supporting the "precipitation membranes" that Moritz Traube had described before him in the walls of a porous pot, in order to give them enough strength to withstand considerable pressure. Such "precipitation membranes" may be produced by the use of many different substances, but the best and commonest one is made by allowing the solution of a copper salt and the solution of a ferrocyanide to move into the wall of a porous pot from opposite sides. They meet in the wall of the pot and a precipitate of copper ferrocyanide is deposited here. The copper solution may now be washed out of the pot and the ferrocyanide rinsed off the outside. In the wall of the pot remains a "precipitation membrane" of copper ferrocyanide. This membrane allows water to pass through it easily, but it will not allow substances dissolved in this water to get through. The membrane is "semipermeable," and therefore is identical in this property with the "osmotic" membrane that Pfeffer maintained surrounded the living cell. If the laboratory cell is filled with a solution of any kind, and is then placed in water, water is sucked into the cell; if it is placed instead in a more concentrated solution, water is sucked out of the cell. As is readily apparent, this corresponds to what Pfeffer and DeVries observed in the case of the living cell.

Pfeffer made many osmotic measurements with his laboratory cell, and, on the basis of his observations, van't Hoff some years later formulated his famous laws, which are as follows:

(1) At constant temperature the osmotic pressure of dilute solutions is proportional to the concentration of the dissolved particles.

(2) At the same temperature equal volumes of all dilute solutions having the same osmotic pressure contain the same number of dissolved particles.

(3) At constant volume the osmotic pressure of any solution varies directly as the absolute temperature.

The work and conclusions of van't Hoff and the physical chemists now became retroactive, and the attempt was made to apply the laws of van't Hoff not only to the biological facts that DeVries and Pfeffer had furnished, but to the additional ones contributed by Hamburger, Gryns, Koeppe, Loeb, Höber, Overton, Webster, etc. To this end the observations made on plant and animal cells were compared with those made with the laboratory osmotic cell. When a solution of any electrolyte or non-electrolyte was found not to change the volume of liquid in an osmotic cell, it was said to be "isosmotic" with the cell contents. Equally

concentrated solutions of all kinds were found to be isosmotic with the contents of the osmotic cell. These were, therefore, isosmotic with each other. When a solution of any kind was found not to change the volume of any living cell it was said to be "isotonic" with the contents of this cell. In this way the solutions of many different substances were compared and the "isotonic coefficients" determined in each case. If the laws of osmotic pressure were active in living protoplasm, it was therefore to be expected that, if certain solutions were "isotonic" with each other, they should also be "isosmotic" with each other.

When the first rough comparisons were made it was in fact thought that the isotonic solutions were isosmotic, but this conclusion could not stand the pressure of more careful and more numerous observations. *To-day we may safely say that we do not know a single cell for which the laws of osmotic pressure are valid.*

We need not go into details to prove this. If cells obeyed the laws of osmotic pressure, then they ought always to have the same volume in isosmotic solutions of different substances. Exceptions to this conclusion are the *rule*. Again, with every increase in the concentration of the medium surrounding a cell we should get a *proportional* decrease in the volume of the cell. As a matter of fact, the shrinkage is always less than anticipated (Koeppe, Durig). While electrolytes and non-electrolytes are in our laboratory osmotic cells equally active when the same number of dissolved particles are present in the unit volume, this is not the case in living cells. Generally speaking, the electrolytes are active out of all proportion to the non-electrolytes when living cells are concerned. How all these facts are readily explained on the colloidal basis has been pointed out above.

To have the laws of osmotic pressure tenable for living cells we must have semipermeable membranes about them. Only as this is the case can changes in osmotic pressure become available for the movement of water into and out of cells. If, for the sake of argument, we grant this conclusion, then no dissolved substances can get into or out of the cell. Such a conception of the cell is impossible, for, under such circumstances, how could a cell get its necessary food, or how could it rid itself of its various metabolic products? To get around this difficulty various observers have made these osmotic membranes permeable to some or many dissolved substances. But the moment we grant this we can no longer maintain differences in osmotic pressure, and so water can no longer be absorbed. The adherents to the view that "osmotic" membranes exist about cells can take their choice: either they can utilize their conception in order to make water move, or they can have these membranes permeable and so have dissolved substances move—but *they cannot have both.*

An enormous literature has sprung up about this question of "membranes" surrounding cells (24). From the original osmotic membranes

of Pfeffer which were semipermeable, we have come to those which are partially permeable, and then to those which are permeable sometimes and then again not. But even these complicated notions encounter trouble, for there is so little connection between the kind of substances that enter cells and those that do not. Only the members of one group—that which has a ready solubility in the fats—have been recognized as having one property in common, and to account for their ready entrance into cells the osmotic membrane about cells has been endowed with lipoidal characteristics. The unfortunate part about this theory, which is in essence that of E. Overton, is that, while it renders easier our conception of the absorption of these lipoid-soluble substances, it makes it impossible to get the ordinary salts and water into cells, for these are not particularly soluble in the lipoids. And yet we know from physiological and pathological facts that both must be able to get into cells.

Moreover, what do we gain when we have succeeded in getting some dissolved substance or water through any membrane postulated to exist about a cell? It would collect here and we should still have to account for the movement of either the dissolved substance or the water into or through the rest of the cell protoplasm. *There are no membranes about cells,* neither of the lipoid type (Durig, 68; Pauli, 67; Fischer, 66), nor of the "osmotic" type (Fischer, 66). All the phenomena which offer so much difficulty in explanation when we assume that membranes exist about cells are readily interpreted, without recourse to such postulates, on the basis of the colloidal constitution of protoplasm as we indicated above.

In answer to these arguments some of our critics have retorted that a "membrane" exists wherever two phases come in contact with each other. At this point we have to stop and begin to define terms, for here the arguments begin to become academic. A drop of any fluid, a drop of any colloidal solution, a drop of protoplasm or a cell, has a "membrane" about it, but this "membrane" is simply a surface tension film; it has nothing in common with the "osmotic membranes" that are in turn talked about by the botanists, the physical chemists, and the original animal physiologists who worked in this field. *These surface tension films are chemically identical with the rest of the cell protoplasm, and* (except as colloidal particles tend to collect in these surface films and so raise the concentration of these particles here) *as such behave toward water or dissolved substances exactly as does the rest of the cell protoplasm.*

We encounter differences in the absorption of water and of dissolved substances in the living animal as we pass from one (colloidal) phase to another. Such different phases may be represented by different organs, different tissues, different cells or intercellular substances, different parts of the same cells. If such phase differences are ultimately shown to exist at the surface of cells, they will assume an importance in this problem

of absorption and secretion. But this importance will be neither greater nor different in this problem, because the phase difference occurs at the surface of the cell than if it had occurred anywhere else in that colloidal complex that we call living matter.

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CHAPTER II

ORGANOTHERAPEUTICS

REID HUNT

INTRODUCTION

Definition.—The term organotherapeutics, as employed at present, can not be very definitely defined. As originally used, it referred to the supplanting, or the supplementing, of the functions of an organ by the administration of the same organ of other animals (lung for diseases of the lung, etc.). The term is now limited to the cases in which the organs in question are believed to form a specific internal secretion. By this limitation the use of extracts of organs producing external secretions was eliminated so far as they were employed for the utilization of the latter (the ferments of the mucous membrane of the stomach, for example). The term is not ordinarily meant to include the supplanting of a deficient organ by transplantation, although here the distinction is often not sharp. In many cases the transplanted organs do not grow, but are absorbed, producing in the course of their absorption the same effects as are produced by the subcutaneous or intraperitoneal injections of the glands.

As knowledge has advanced the term has been made to cover more in some, and less in other, directions. With the isolation of "active principles" from organs (epinephrin from the suprarenals, for example), the use of the latter in some conditions no longer differs from the use of ordinary drugs; thus the conception of organotherapeutics is narrowed. On the other hand, it is being recognized that some of the effects of well known drugs are due to specific actions upon organs of internal secretions. Some of the effects of iodin, for example, are due to the fact that it increases the amount or potency of the internal secretion of the thyroid (Hunt, 100). There is evidence that certain foods also increase the activity of some organs of internal secretion (Hunt, 101). In principle it makes little difference whether the internal secretion is introduced from without or formed within the body. In this sense the conception of the term may be enlarged.

For present purposes organotherapeutics may be defined as the utili-

zation for therapeutic purposes of internal secretions, or hormones, in cases where these are deficient.

Limitations of Organotherapeutics.—Organotherapeutics is one of the oldest and most widespread forms of therapeutics. After many centuries of empiricism, during which not a single result of value was obtained, it almost disappeared, except in popular and sectarian medicine. It was revived by Brown-Séquard in 1889. Its recent development, especially on the part of manufacturers, has been not unlike that of ancient times.* Physicians, however, have for the most part limited their attention to organs which are believed to produce internal secretions; in this way modern organotherapeutics rests upon a new basis. The older organotherapeutics was based on the belief that it was possible to influence certain diseased organs by the administration of healthy organs; modern organotherapeutics is concerned, primarily, not with the condition of the organ diseased, but with the activities of other organs which are impaired by the absence or diminution of an internal secretion. Thus thyroid is not given primarily for its effect upon the thyroid gland, but for its effect upon various other organs whose activities are in part dependent upon the internal secretion of the thyroid.

Recent experimental and clinical work in this field has accordingly been directed to two chief aims: the demonstration that various organs produce internal secretions, and attempts to determine the conditions under which these may be utilized for therapeutic purposes.

Great progress has been made in the former attempt; it has been shown that many organs produce internal secretions essential to life or to the proper fulfillment of certain functions.

Much less progress has been made in the utilization of these internal secretions, and we are only beginning to be able to explain the cause of some of the failures.

Some of the general principles underlying success in organotherapeutics are being recognized. Thus, it is self-evident that, however important the internal secretion of an organ may be, no results can be expected from the administration of this organ unless it has the property of retaining or storing some of its secretion; attempts have been made for years to use organs for therapeutic purposes, which recent investigations seem to show have not this property. Hence, it is very important to determine to what extent the internal secretions are stored in the organs producing them, and how much is necessary to maintain health. This is possible, in a general way, in the case of a few organs. Thus, from studies on the amount of thyroid which it is necessary to administer

* Two hundred and sixty-seven glandular products were recently found listed in trade journals. The lists included brain, spinal cord, liver, kidney, etc., and did not differ greatly from the lists of a century or two ago; the chief difference is that the "indications" are expressed in more modern but none the less obscure phraseology.

to animals or man suffering from removal or disease of the thyroid to maintain health, it is possible to form an approximate estimate of how much thyroid secretion is necessary, and from the weight of the gland how much of the material is stored in it. Such calculations show that the thyroid contains sufficient secretion to meet the demands of the body for several weeks. From a determination of the amount of epinephrin (one of the internal secretions of the suprarenals) contained in the blood of the suprarenal vein, and from the rate of blood flow through the suprarenal glands, it is possible to make a rough estimate of the amount of epinephrin produced (and presumably needed) daily; when this amount is compared with that actually found on chemical analyses in the suprarenal glands, it is found that the latter is not sufficient to meet the needs of the body for more than a few hours. Since some of the internal secretion is almost inevitably lost in the manipulations necessary to prepare the gland for administration, it is evident that the conditions in the case of the thyroid are far more favorable for success than in the case of the suprarenals. (Other reasons for expecting far more success from thyroid than from epinephrin will be discussed later.)

Although there is little doubt that the pancreas forms an internal secretion essential to life, all attempts to demonstrate its presence in the gland have failed. The secretion seems to pass into the blood as rapidly as it is formed, or, if some of it is retained in the gland, it seems to be in a condition not suitable for therapeutic purposes.

In addition to knowing how much of the secretion is stored in the gland, it is important to know how urgent is the body's need for the secretion, and how long the latter remains in the body. Light on these questions has been obtained by determining how soon symptoms appear after the removal of the glands. Taking two extremes, it has been found that symptoms may not appear for weeks after removal of the thyroid, whereas they appear within two or three hours after removal of the pancreas. It is evident that the chances for successful treatment are much more favorable in the former case.

Another important consideration is the character of the internal secretion, its resistance to the manipulation necessary to prepare it for administration, the effect of digestive juices upon it, its absorbability, etc. Here, again, there are marked differences. The active principle of the thyroid, or rather a product derived from the thyroid and having its physiological properties, resists the action of strong chemical agents and of the digestive juices, and it is readily absorbed from the gastrointestinal canal. Epinephrin, on the other hand, is a comparatively unstable body which is absorbed from the gastrointestinal tract, in effective amounts, very slowly.

Another suggestion offered in explanation of the failure of attempts to use some of the organs for therapeutic purposes is that the internal

secretion is not always produced in an active form—that it may be produced in a form analogous to a zymogen, for example, which requires "activation" by some other organ; or it may be impossible, practically, to administer the internal secretion so that it will reach essential organs in efficient concentration. Recent work by Hédon (88) on the internal secretion of the pancreas is suggestive in this connection: Hédon found that, when the blood from a pancreatic vein was introduced into the portal circulation of a diabetic animal, there was a diminution of the glycosuria; it had no effect when introduced into the general circulation. Thus, it seems necessary, for some reason, for the internal secretion of the pancreas to reach the liver in order that it may be active.

The above illustrations show some of the ways in which experimental work is elucidating the problems of organotherapeutics. There are so many unknown factors, however, that actual clinical trials are, and must remain, the final test for the value of this form of treatment in any specific case; but, when favorable clinical reports are made in cases, as with the pancreas, where there are so many experimental reasons for doubting the efficacy of present methods, it is incumbent upon those making such reports to carefully exclude all other factors.

Skepticism as to reports of success in organotherapeutics is thoroughly justified; for it must be recognized that under the most favorable condition the normal processes can only be most imperfectly imitated. In the normal animal the secretion is under the control of delicate mechanisms (frequently of the nervous system), by which it is supplied at the proper time and in the proper amounts; such a regulation is impossible when the internal secretions are administered medicinally.

Classification.—At present the only practical method of classifying organotherapeutic products is by the organs from which they are derived. Such a classification, however, is already too narrow, and, with the further growth of knowledge, will probably have to be abandoned altogether. One or two illustrations will suffice: Among the symptoms of suprarenal insufficiency are low blood pressure and an enfeebled heart, due to the diminution of one of the internal secretions which normally maintain cardiovascular tone. This insufficiency may be met by the administration of suprarenal extract. But the latter is equally effective in conditions of hypotonus occurring entirely independently of the suprarenal glands. The same is true of an entire system, viz., all the organs innervated by the sympathetic nervous system. This particular secretion of the suprarenal (epinephrin) may be classed as a "sympathomimetic" (Barger and Dale, 12) drug; i. e., a drug the action of which is similar to that of sympathetic nerves. It belongs to a class including many other (mostly new) drugs. Thus, it passes from the present classification altogether. As knowledge advances, this will probably be the case with most of the substances now treated under the head of organotherapeutics.

THYROID

The employment of the thyroid in medicine is a typical case of substitution therapy, for the functions of the gland may, in favorable cases, practically be replaced by the administration of the gland. So well established is this principle that physicians do not hesitate to diagnose conditions of the thyroid from the effects of the administration of the gland.

The administration of the thyroid in organotherapeutics is based partly upon clinical and partly upon experimental work. The latter preceded the former,* but from almost the beginning the two methods have been closely combined, each reacting upon the other. The gland was not employed in medicine until a rational basis for its use had been established; empiricism had no part in its introduction.

The basis for its use will be made most clear by a brief review of the development of the knowledge of the physiology of the gland.

Functions of the Thyroid

It is not necessary to refer to the various views as to the function of the thyroid held previous to the years 1882-83, for these years mark a most important epoch in the subject. It was then that J. L. and A. Reverdin and Kocher (112) published the results of their observations upon patients from whom the thyroid had been removed, and which gave the first real insight into the importance of the gland. Schiff had in 1859 published a brief statement upon the effects of removal of the "thyroid" in dogs, but it had not received much attention, and it is now recognized that the symptoms described by this investigator were largely due to the removal of the parathyroids, which are now generally regarded as glands with functions quite different from those of the thyroid. It had also been recognized that the thyroid presents anomalies in cretinism, and a connection had been suggested between the thyroid and myxedema. Kocher designated the condition of the patients from whom the thyroid had been removed as *cachexia strumipriva*.

These clinical observations led to extensive series of experiments on animals by Schiff, Horsley, and many others. These soon removed all doubt as to the cause of the symptoms described by Kocher and the Reverdins. Within a few years following the publications of the latter, it was recognized that the underlying cause of cachexia strumipriva (or thyreopriva), sporadic and endemic cretinism, and of myxedema was the same in all, namely, the deficiency or absence of the thyroid. The

* The first attempts to combat thyroid deficiency were the transplantation experiments in dogs by Schiff; these were the direct stimuli to similar experiments in man.

characteristics of the symptoms are largely dependent upon the age of the animal or patient at which the thyroid is removed or becomes inefficient. The results of the extirpation experiments have been much confused by the fact that some of the parathyroids were frequently removed with the thyroid. The differences in the effects of thyroidectomy in different species of animals are due, at least in part, to the fact that the anatomical relations are such that the parathyroids are more likely to be removed in operations on some animals than on others, and also to the presence, in varying numbers and locations, of accessory thyroids which may at least partially take up the function of the thyroid.

The careful study of the effects of the removal of the thyroids, especially of their removal from young animals or from young patients, and of the above-mentioned pathological conditions, has thrown much light on the function of the gland; and the knowledge thus obtained, combined with that obtained by administering the gland, in various ways, to patients and animals, serves as the basis for the use of the thyroid in therapeutics. A brief summary of the facts thus learned will be given.

Relation of Thyroid to Growth and Development.—The most marked effect of the removal of the thyroid in young animals, and of its atrophy or injury in children, is a cessation of growth and development, both physical and mental. The changes in the skeleton are especially marked;* there is a cessation or retardation of the normal ossification of the cartilages. The epiphyseal ends of the long bones grow slowly, while the periosteal ossification may be normal or in excess. The extremities are relatively short and thick; the pelvis is small, which is partly responsible for the protruding abdomen. Abnormalities in the growth of bone are largely responsible for the characteristic shape of the skull and thorax in cretins.

If the thyroid deficiency does not occur until rather late in childhood, the above changes may be absent, and the hypothyroidism be evident only in a cessation of normal growth.

The hair on the pubes and in the axillæ is scanty or absent, and the sexual organs are poorly developed; while puberty, if it occurs at all, is late. The skin is often myxedematous. Metabolism is much depressed (v. Bergmann, 214); the oxygen absorption may be but one-half that of the normal.

It is difficult, however, to distinguish between primary and secondary effects of injuries to the thyroid. The latter cause marked changes in nutrition and metabolism, and these may be the immediate cause of some of the abnormalities now ascribed to the direct influence of the thyroid.

The effects of thyroid insufficiency upon mental development are no

*** See, for example, Flinker (59); the opposite changes are found in conditions of hyperthyroidism in young individuals (Holmgren, 93).**

less striking than are those upon physical development; the patients are apathetic, the expression is stupid, and idiocy frequent.

Thyroid Deficiency in Adults.—Thyroid deficiency in adults is seen most typically in myxedema, which is characterized by physical and mental inertia, and by changes in the skin, depressed metabolism, etc. The skin is white and thickened, due to the growth of granulation-like tissue and an infiltration with a substance resembling mucin; the secretions are scanty or absent, and the skin becomes dry and rough, and the hair falls out. There are frequently abnormal sensations of taste, smell, and hearing.

The temperature is subnormal, and the pulse slow and weak. There are diminished oxygen absorption and carbon dioxid secretion; there is a tendency to obesity, although the patients usually eat little. The metabolism is depressed to a greater degree than in any other known condition. Andersson (6) reports a case of a woman whose metabolism was as low as 1,260 calories, or 18.8 calories per kilogram. After treatment for nine months with thyroid extracts, the heat production rose to 2,099 calories, or 32.3 per kilogram, which are normal values.

Nitrogen metabolism is also lowered; the daily excretion of urea is often less than 20 grams.

Lusk (132) states that it is possible to explain the reduced temperature as due to disturbances in the nervous mechanism of temperature regulation, and that the lowered temperature may be an influence in reducing the metabolism of the cells. The coagulation time of the blood is stated to be shortened (Lidskey, 123).

Thyroid Deficiency in Animals.—The effect of thyroidectomy in animals is variable; much depends on the age. Monkeys may show a condition very analogous to myxedema in human beings. Many adult animals show little change after removal of the thyroid, although eczema, conjunctivitis, rhinitis, and other indications of catarrh of the respiratory passages; and especially emaciation and diminution in the number of the red and increase in the number of the white corpuscles are common. Metabolism is depressed, carbohydrate tolerance is increased. Marked changes are found in the hypophysis (Rogowitsch, Herring).

Effect of the Administration of Thyroid.—The most marked effects of the administration of thyroid are seen in cases in which the thyroid is absent or deficient, and it is upon the results in such cases that the therapeutic use of thyroid is largely based.

Administered to cases of sporadic cretinism and infantile myxedema, there is at first a loss of weight, then the skin approaches the normal. Cyanosis disappears, and the blood becomes normal. Growth, both bodily and mental, recommences, and may take an almost normal course. The hair grows rapidly and becomes glossy; the teeth and nails also grow. The mental improvement is most marked in children under ten.

Similar results are obtained in cretinoid animals (Pick and Pineles, 171).

From these results it is concluded that the thyroid produces an internal secretion necessary to normal growth. Many attempts have been made to stimulate growth in conditions other than cretinism by its administration. Thus, it has been extensively tried in idiots and backward children. It has been administered in cases of delayed union of fractures on the theory that it would hasten union.

Administered to cases of myxedema or cachexia thyreopriva, the myxedematous condition largely disappears. There is a marked increase in both nitrogen and gas metabolism. The excretion of nitrogen in the urine may be increased 100-200 per cent. This increase results largely from the increased intake due to improved appetite, but there is usually a true loss of nitrogen. There are no striking changes in the partition of the nitrogen in the urine. The consumption of oxygen may be increased 70 per cent. The temperature rises, the pulse rate is increased. There is usually a striking loss of weight due to the disappearance of the myxedematous infiltration and loss of fat. The entire metabolism is brought back to the normal level, or raised slightly above the normal. These changes occur in three to four weeks with the usual doses.

The skin approaches the normal; sweating, which is usually entirely absent in myxedema, becomes possible. The hair grows again. Menstruation reappears. The bowels become regular. The mental condition is much improved.

The marked changes in the skin in cases of myxedema produced by the administration of thyroid has led to the extensive trial of this substance in other abnormal conditions of the skin.

Effects upon metabolism similar to, but much less marked and less constantly obtained than, the above are produced when thyroid is administered to normal individuals and to normal animals. The absorption of oxygen and the excretion of carbon dioxid may be increased 10 to 20 per cent., although in some cases there is no increase. The excretion of urinary nitrogen may be increased 20 to 50 per cent.; usually it is less, much depending on the character of the diet. The change in nitrogen metabolism usually occurs first; that in total metabolism occurs later (in the course of two to three weeks). Increased destruction of protein can not always be prevented by the administration of non-nitrogenous food.

The excretion of phosphorus and of sulphur is also increased.

No other organ has such marked effects upon metabolism, and many attempts have been made to utilize these effects therapeutically.

The indications for the use of thyroid are clear in those cases in which there is a deficiency of the normal secretion; in other cases, however, its administration must be largely determined empirically, for the

mode of action of thyroid upon metabolism is obscure. Some believe that it stimulates cells directly to increased activity; whereas others think that the effect is primarily upon various parts of the nervous system, the stimulation of which causes increased activity which results in increased metabolism. In support of the latter view Andersson and Bergmann (5) state that there is no increase in the carbon dioxid output when thyroid is administered to a man kept in perfect quiet. That excessive amounts of thyroid do increase nervous irritability is generally accepted on the basis of observations in Graves' disease, and the results of administering large doses of thyroid. Magnus-Levy (136) believes that there are great individual differences, but that in some cases there is an increased metabolism of the resting cells. It is evident that the solution of this problem has important bearings upon the use of thyroid to influence metabolism; if the thyroid increases metabolism only indirectly by causing, through stimulation of the nervous system, increased activity, it could scarcely be considered a specific treatment of obesity, for example (at least in those forms in which thyroid deficiency is not a causal factor).

Excessive doses of thyroid have marked effects upon the circulation and nervous system, but these are of interest chiefly in connection with the toxic action of the drug; they do not suggest any therapeutic use for it. Eppinger, Falta, and Rudinger attribute many of these effects to increased irritability of the sympathetic nervous system.

Therapeutic Uses of Thyroid

Thyroid is employed both rationally and empirically. In all cases where the pathological condition is clearly due to thyroid deficiency the treatment gives brilliant results, unless serious secondary effects or complications have arisen. Its empirical use has not, in most cases, been attended with much success.

Conditions of Hypothyroidism (217, 222).—For the use of thyroid in hypothyroidism, see Vol. III, Sec. IV, Chapter VII.

Mild Conditions of Hypothyroidism.—In addition to the above conditions, in which there is obviously severe thyroid deficiency, there are a number of conditions of hypothyroidism of a less severe type; Hertoghe and Kocher (114) have laid especial emphasis upon these. Kocher states that he sees many cases which have been treated for anemia, chlorosis, scrofula, nervousness, and disturbances of menstruation, which seem to him clearly to be cases of thyroid deficiency. He also calls attention to the cases in which children show retarded growth with no apparent cause. The favorable results following the administration of thyroid makes the diagnosis of the condition clear. Many of the cases of mild thyroid deficiency show, according to Kocher, very definite symptoms, among

the most marked of which is a feeling of inhibition preventing the subjects from accomplishing that which they desire. They are incapable of continued effort, such as reading, writing, and even speaking; they become shy and avoid society. They are indifferent to food, and neglect going to stool.

The author states that remarkable improvement follows the administration of thyroid in such cases.

Kocher mentions many other symptoms due, as the effect of thyroid treatment shows, to slight thyroid deficiency. Among these are fatigue from slight exertion, although muscular development is good; slight swellings of the eye-lids, lips, and cheeks; tendency to obesity, and the appearance of local accumulations of fat; swelling of the joints, so that patients frequently state that they suffer from gout or rheumatism; paresthesias, especially feelings of stiffness. Sometimes the skin has a yellowish tinge, suggesting chlorosis. Pigmentation of the skin is frequent, resembling that seen in pregnancy; the pigmentation in the latter condition may be due to relative thyroid insufficiency. This pigmentation often disappears under the influence of thyroid.

The author raises the question if the effect of the thyroid in such cases may not be due to an effect upon the suprarenals or other organs of internal secretion.

Further changes in the skin and its appendages, upon which Kocher lays much emphasis, are dryness and coldness, with little tendency to sweating; the dryness of the hair and its tendency to fall out; the tendency of the nails to crack, and of the teeth to caries.

The author warns against ascribing more severe skin diseases to a condition of hypothyroidism, although he states that eczema, ichthyosis, etc., are especially prone to occur where the nutrition of the skin is deficient as a result of hypothyroidism.

Individuals with these mild degrees of hypothyroidism are sensitive to the cold. The coldness of the skin is due to sluggish circulation, which is also evident from the slow, weak pulse.

Kocher states that marked improvement occurs in such cases as the above within a week or ten days, sometimes even in twenty-four hours, after beginning the administration of thyroid. Similarly beneficial results are stated to occur in the aged, when symptoms of thyroid hypofunction result from the gradual deterioration of the gland, and in pregnancy, when the thyroid is unable to meet the increased demands made upon it.

Various chronic diseases and intoxications (tuberculosis, alcoholism, and sometimes syphilis) may injure the thyroid, so that a mild degree of hypothyroidism results; here again thyroid medication may be of benefit.

Stoeltzner (205) states that rudimentary forms of infantile myxedema, characterized by cessation of growth, excessive fatness, etc., are not uncommon; they sometimes follow infectious diseases or traumatism. Thyroid causes much improvement. Simpson (200) reports favorable results in many cases of infantile wasting. For children under nine months he began with one-third of a grain of the dry gland once daily, larger doses sometimes causing diarrhea. Doses up to 1 grain daily were given to older children.

Goiter (115, 152).—For the use of thyroid in goiter, see Vol. III, Sec. IV, Chapter VII.

Obesity.—For the use of thyroid in obesity, see Vol. II, Sec. III, Chapter VII. (See also references 67, 133, 136, 137, 149, 163, 183, 214, 218, 219, 220.)

Other Conditions.—In addition to the above, thyroid has been given in a very great number of other conditions. In some of these thyroid deficiency was suspected; in others it was apparently used because the symptoms resembled some of those occurring in hypothyroidism. Among these conditions are various *disturbances* of the *skin*, especially the dry, scaly varieties; thus it has been highly recommended in eczema, especially in that of early childhood and of old age. It has been used extensively in psoriasis, chronic urticaria, pruritus, pemphigus, ichthyosis (Roux and Galippe, 189), and scleroderma (Rocques, 184); in the latter condition the thyroid has sometimes been found atrophied (Wells, 224).

It has been recommended in various disturbances of the joints, such as *arthritis deformans*, irregular gout, chronic *rheumatism*, and indefinite "rheumatoid" pains (Steele-Perkins, 202; Wilson, 231; Stubenrauch, 206). Among recent writers Lévi and Rothschild (122) have especially emphasized its value in certain forms of rheumatism of children; in these the thyroid is frequently enlarged (Clemens, 38). It has also been used in certain cases of migraine and neuralgia, especially in those associated with menstruation. Thyroid has found extensive use in various disorders of *menstruation* (Goodall and Conn). Experimental and clinical work has shown that the thyroid is necessary for the proper development of the genital organs and for menstruation. Further relations between the thyroid and the female sexual organs are suggested by the more frequent occurrence of myxedema in women after the climacteric, especially in those who have borne children, the more frequent occurrence of exophthalmic goiter in women, and by the enlargement of the thyroid during menstruation and pregnancy. It has been recommended in amenorrhea when other causes can not be detected, and especially if there is a tendency to obesity or myxedema. Thyroid in large doses has been warmly recommended in *eclampsia;* the beneficial effects were attributed in part to the diuretic action.

The influence of the administration of thyroid upon the defective growth of bone in cretinism suggested its use in *delayed union* of *fractures;* some writers have reported very favorable results. Bircher (28) found that the administration of thyroid to young animals delayed bone growth; he does not believe that the effect in cretinism is specific. Thompson and Swarts (209), contrary to some, did not find that removal of the thyroid delayed the healing of fractures. It has been said to give good results in rickets (Variot and Pironneau, 211).

Excellent results have been reported from the use of thyroid in *hemophilia* (Rugh, 190). It is said that the preliminary administration of the drug renders necessary operations (extraction of a tooth, for example) safer. Such results would scarcely be expected, for the coagulation of blood is said to be distinctly delayed in Graves' disease and experimental hyperthyroidism (and to be accelerated in conditions of hypothyroidism).

The marked mental changes produced by the administration of thyroid in myxedema and cretinism have led to the use of thyroid in other *mental disturbances;* the results in certain cases of beginning melancholic insanities are stated to have been good. It is interesting to note in this connection that a very large percentage of patients who die with mental diseases have abnormal thyroids (Peabody, 167), and that Grafe (77) has found in certain mental diseases a true retardation of metabolism (heat production 39 per cent. below normal, for example), which is suggestive of a condition of hypothyroidism.

Methods of Administering Thyroid

Transplantation.—The earliest attempts to combat thyroid deficiency were by the transplantation of normal thyroid. This method has succeeded when the thyroid was transplanted to another part of the same individual. It has been less successful when the gland was transplanted from one animal to another of the same species. It is especially recommended in cases in which other forms of substitution therapy fail. Kocher states that one great advantage of transplantation is that the body can regulate the amount of secretion according to its needs.

Subcutaneous Injections.—Murray (1891) introduced the method of treating myxedema by the subcutaneous injection of glycerin extracts of thyroid; the extracts were obtained from sheep and calves, and were preserved with phenol. They frequently caused severe local reactions. Beebe has recently suggested that this method be revived; he recommends the use of a preparation of thyreoglobulin.

Administration by the Mouth.—A very important advance in thyroid medication was made in 1892, when Fox, Mackenzie, and Howitz almost simultaneously announced that favorable results could be obtained in

myxedema by the administration *per os* of the fresh or cooked thyroid. The use of cooked glands was soon practically replaced by the use of the dried glands, and of various extracts. Some of these have received recognition in various pharmacopeias.

Chemistry of Thyroid

The older investigators reported the presence in thyroid of albumins, nucleoproteids, albumoses, leucin, xanthin, hypoxanthin, lactic and succinic acids, etc. In glands which have undergone cystic degeneration the finding of mucin, cholesterin, methemoglobin, bile pigments, etc., is reported.

Since the discovery, in 1895, by Baumann (16) of iodin in the thyroid, interest in the chemistry of the gland has centered largely around this element, and the substances with which it is in combination.

The amount of iodin in the thyroid, not only of man, but of the lower animals, is extremely variable, being influenced by age, character of the food, locality, and many other, for the most part unknown, factors. The thyroids of infants and of newly born animals contain little iodin; in fact, it can not be detected at all in many cases, at least not by the use of usual quantities of the gland, and by the usual methods. Aschbacher gives the average amount of iodin in the human thyroid between the ages of twenty-five and thirty as 8.98 milligrams; it is less both in youth and old age. The percentage based on the weight of the dry gland varies from zero to 0.4 or 0.5. Extreme variations both in the total amount and in the percentage occur.

The form of combination of iodin in the thyroid is unknown, notwithstanding the large amount of work which has been devoted to the problem. The form is specific for the thyroid; no other iodin compound is known which has the physiological properties of the thyroid substance (Hunt and Seidell, 104). It is known to be united in some way to the proteins, probably to one or more of the amino acid constituents of these.

Baumann isolated a specific but ill-defined iodin compound from the thyroid, one which has at least many of the peculiar properties of the gland substance itself. He named this substance iodothyrin.

Oswald (159, 160) isolated, at least approximately, the protein with which the iodin is combined. He named this protein thyreoglobulin; it was found to constitute one-third to one-half or more of the weight of the dry gland. The iodin content varied from zero to 0.86 per cent. or more. Oswald believed this thyreoglobulin, when it contained iodin, to represent the true active principle of the thyroid; Baumann's iodothyrin could be obtained from it by hydrolysis.

Oswald also isolated an iodin-free protein having the properties of

a nucleoproteid; this did not have the characteristic physiological thyroid action.

Beebe (18), using similar methods, did not secure as complete a separation of iodin-containing and iodin-free proteins.

Relation of the Iodin to the Physiological Activity of Thyroid.— Baumann's discovery of iodin in the thyroid stimulated an immense amount of work, and led to the accumulation of a large number of facts as to the occurrence of iodin in the thyroids of various animals, and in those of man, under various conditions, both pathological and normal. The fact that iodin can frequently not be detected in the thyroids of healthy individuals has led many to doubt whether this element is a necessary or important constituent of the gland (c. f. Hunt and Seidell, 102). From almost the beginning there has been evidence, not very conclusive, however, that the activity of the thyroid when used as a drug is closely dependent upon its iodin content. Thus, Roos (186) in three experiments upon dogs found that more nitrogen was excreted after the administration of thyroid rich in iodin than after that of thyroid containing little iodin. Roos also administered thyroid containing different amounts of iodin to four patients with parenchymatous goiter; that containing the largest amount of iodin was the most active in diminishing the size of the goiter.

Oswald (157, 158) also found in two experiments thyreoglobulin rich in iodin to cause a greater excretion of nitrogen than did thyreoglobulin poor in iodin. Marine and Williams (139) found in two experiments that thyroid containing a larger percentage of iodin caused a greater loss of weight in dogs than did a preparation containing a smaller percentage.

Hunt and Hunt and Seidell, in extended series of experiments, in which the effect of thyroid upon the resistance of animals to certain poisons was determined, found a close parallelism between the physiological activity of the thyroid and its iodin content. They also found that the iodin which accumulates in the thyroid after feeding iodin compounds is present in an active form, that is, in the form characteristic for the thyroid.

Although further clinical tests are desirable, the above experiments offer almost conclusive evidence that the therapeutic value of thyroid is directly proportional to the iodin content (Kocher, 113).

Several writers have called attention to the variations in the iodin content of commercial thyroid preparations; Hunt and Seidell found the preparations on the American market to vary from 0.095 to 0.38 per cent. The average was approximately 0.2 per cent.

It is thus evident that the commercial preparations vary by as much as four hundred per cent. Such variations in the strength of most drugs would be considered intolerable, and there can be little doubt that more

satisfactory results would often be obtained if the thyroid preparations were more uniform in strength. That lack of uniformity does not cause more inconvenience is due largely to the fact that thyroid medication must, by its nature, be peculiarly individual; the dose must be governed by the degree of thyroid deficiency of the patient, and this can only be determined by trials of different doses. When, however, the proper dosage of a certain preparation in an individual case has been determined, it would be distinctly advantageous to be able to continue the same dosage if a fresh supply were prescribed; at present, even if the same firm's preparation were prescribed, the second order might be several times as active as the first. Hence, it would be very desirable for the pharmacopeia to fix a standard iodin content for the official preparation; a standard of 0.2 per cent. would seem reasonable (Hunt and Seidell, 103).

Official and Other Preparations of Thyroid

Pharmacopeial Preparations.—Desiccated thyroid gland is recognized in the United States Pharmacopeia (VIII, 1905) under the name Glandulæ Thyroideæ Siccæ; it is directed to be obtained from the sheep and to be freed of fat, and powdered; one part represents approximately five parts of the fresh glands. Tests are included to insure the presence of iodin in organic combination and the absence of inorganically combined iodin. The average dose is given as 0.25 gram, or four grains.

The Belgian Pharmacopeia (III, 1906) recognizes thyroid in various forms. It is stated that sugar of milk should be added to the dry thyroid or its extracts, so that the weight equals that of the fresh gland from which it is obtained; a gram of the fresh gland or the equivalent in the dried or extracted form contains about 0.0003 gram of iodin. This corresponds to about 0.15 per cent. iodin in the dried gland.

The British Pharmacopeia (1898) recognizes two preparations of thyroid, the dry (Thyroideum siccum) and the solution (Liquor Thyroidei). The former is directed to be dried at 32.2° C. to 37.8° C. and to have the fat extracted; the dose is given as three to ten grains. The solution is prepared by macerating the glands (of sheep) with equal parts of glycerin and a 0.5 per cent. solution of phenol, straining and adding sufficient of the phenol solution to make six c. c. for each entire gland used. It is to be freshly prepared; dose, five to fifteen minims (which is equal to one-sixth to one-twentieth of an entire gland).

Tablets.—At present thyroid is administered, at least in this country, chiefly as the dried powder which is usually prescribed in the form of tablets. Such tablets are very convenient and satisfactory if they are well chewed, but their use has led to the utmost confusion as to dosage. Many physicians both here and abroad speak of prescribing so many

"tablets" without, as a rule, specifying either the size of the tablet or the maker; others speak of prescribing "two" or "five-grain tablets," without specifying whether the weight refers to the total weight of the tablet (that is, the thyroid plus the excipient), or to the thyroid alone, and, in the latter case, as to whether the weight refers to the fresh or dry gland. Others specify some manufacturers' "tablets" without further particulars. How inexcusably inexact are such procedures is evident from such facts as the following: Many manufacturers prepare several "tablets" of different sizes; one firm, for example, lists "one-half, one and one-half, two and one-half, and five-grain, and one-tenth and three-tenths-gram tablets"; which of these tablets the patient received when the physician states that he administered this firm's "tablets" it is usually impossible to determine.

The confusion as to dosage is still further increased by the fact that different firms use different methods of expressing the amount of thyroid in their tablets. Thus, one firm's "five-grain tablet" contains two grains of desiccated thyroid; another firm's "five-grain tablet" means that each tablet contains the equivalent of five grains of the fresh gland. One firm's "two-grain tablet" means that each tablet is equivalent to ten grains of the fresh thyroid; another firm states that one grain of their dry thyroid represents eight grains of the fresh gland. There can be little doubt that, when some physicians write of prescribing a five-grain tablet of dry thyroid, they really prescribed a tablet containing the equivalent of five grains of fresh thyroid, or one-fifth of what the reader may be led to suppose.

Since some commercial "tablets" contain twenty times as much thyroid as other "tablets," and since some preparations of thyroid are four times as active as others, there is a *possibility* of one "tablet" being equal, physiologically, to eighty other "tablets." *

Extracts and Other Preparations.—In addition to the above, there are a number of extracts and other preparations of the thyroid on the market. The term "extract" is frequently applied to the dried powder, a practice often leading to confusion.

Thyroidin-Merck, a preparation to which reference is frequently made in the literature, is dried thyroid, four-tenths gram of which is equivalent to one fresh sheep thyroid of medium size; one part represents about six parts of the fresh gland.

Thyreoidin-Notkin is a preparation of the proteins of the thyroid, stated to be especially useful for hypodermic injection. The dose *per os* is one-sixth of a grain; hypodermically, 15 minims of a five-tenths per cent. solution.

* The above remarks apply to the tablets on the American market. Equally great confusion prevails in regard to other "tablets" on foreign markets; thus in one case a one-tenth-gram tablet contains one-fourth of a medium sized thyroid of a sheep.

Thyraden is the extract prepared by extracting the glands with normal saline solution and precipitating the proteins and drying. It contains 0.07 per cent. iodin; one part is equal to about two parts of the fresh gland.

Beebe (18) has recently proposed the use of *thyroid proteins* (thyreoglobulin) prepared by extracting the ground glands with normal saline solution and precipitation with acetic acid at 44° C.; the proteins are to be dried and mixed with sugar of milk in such proportions that the preparation contain 0.338 per cent. iodin.

Iodothyrin.—As has already been stated, Baumann obtained from the thyroid a substance rich in iodin, which he called iodothyrin.

Both clinical and experimental studies with iodothyrin have led to very contradictory results. Some of the earlier writers reported finding iodothyrin to have the full activity of a corresponding amount of thyroid, or to be even slightly more active than this; many later writers have found it very inferior to the latter.

Some of the latter results are doubtless due to the employment of too small doses. This seems to have been the case, for example, in the experiments of Pick and Pineles (170), who concluded that iodothyrin is entirely incapable of replacing thyroid. An examination of their paper, however, shows that they compared the effects of from 0.3 to 0.9 grams of the commercial "iodothyrin" with that of from 1.4 to 3 grams of dry thyroid; the above doses of "iodothyrin" correspond to 0.3 to 0.9 gram of the fresh thyroid, or to about 0.06 to 0.18 gram of the dry gland. These authors thus fed about twenty times as much of the one preparation as of the other.

Other of the negative results with iodothyrin were probably due to the use of inferior preparations. Hunt and Seidell (104) found two of three commercial preparations to contain loosely combined iodin; one of these was almost inert physiologically, the other had a moderate degree of activity, whereas the third preparation, which gave no reaction for loosely combined iodin, was as active as thyroid containing a corresponding amount of iodin.

The above considerations explain some of the contradictory statements concerning the therapeutic efficiency of iodothyrin. Possibly other factors are involved. von Noorden (219) states that he has abandoned the use of iodothyrin (in obesity), because it did not seem sufficiently effective in the customary doses (one gram daily), whereas, with doses of two to three grams, which had a definite effect on body weight, patients complained of irritation of the heart. Kocher (114) states that he has seen cases in which ordinary thyroid preparations failed, but in which iodothyrin succeeded, and *vice versa;* he also cites a striking case of cachexia thyreopriva in which the symptoms were completely relieved both by iodothyrin and by thyroid extract.

Untoward Effects and Contraindications

Untoward effects not infrequently follow the medicinal use of thyroid. There are, however, great individual differences in susceptibility. Children are stated to be less sensitive than adults; patients with myxedema and goiter are especially sensitive.

Among the milder symptoms reported from overdoses, or the long-continued use of smaller doses, or in especially sensitive individuals, are flushing with increased sweating, fullness of the head with palpitation of the heart, tachycardia and anginose pain in the heart, dyspnea, faintness, dizziness, loss of appetite, etc. Such symptoms have followed the taking of two grains of the dry powder. Other symptoms are nausea, vomiting, and severe diarrhea. Foulis reported a case of profuse fatal diarrhea following the first dose of one-fourth of a lobe of thyroid in twenty-four hours. Glycosuria frequently occurs. Marked nervous disturbances may occur. In addition to the palpitation, etc., there may be great restlessness and sleeplessness, irritability, tremors, pains in the back and extremities, and even delirium. The temperature is sometimes elevated. Urticaria and other disturbances of the skin may occur. Great emaciation, long-continued debility, and anemia have been reported; the urine may be diminished, although, as a rule, thyroid has a diuretic action.

In cases of rapid growth under treatment, bow-legs have sometimes been reported; in such cases the dose should be immediately diminished.

A number of fatal cases have been reported from ordinary or small doses.

A condition very similar to exophthalmic goiter has been reported a number of times following the excessive use of the drug. Von Notthaft (221) reported such a case where an obese man took nearly one thousand "tablets" in five weeks; the symptoms slowly subsided when the drug was discontinued.

A large number of accidents, some of them fatal, have occurred from the use of thyroid in obesity. It is especially dangerous in obese patients with a tendency to cardiac or aortic disease. It is also contraindicated in obese patients with a tendency to diabetes.

Beebe (17) reported a case of fatal diabetes in a woman after recovery from Graves' disease following the administration of thyroid.

Crile (42) states that death has followed a single therapeutic dose of thyroid in Graves' disease. Kreeke reports that he has seen emaciation, tachycardia, and excitement continuing for a year after the administration of thyroid to patients with Graves' disease.

THE PARATHYROID GLANDS

Functions of the Parathyroid Glands.—What is known of the functions of the parathyroids has been learned almost entirely from the extirpation of these glands in animals and man. The typical symptoms in animals are as follows: There is a latent period of several (twelve to forty-eight) hours in which the only symptoms may be a loss of appetite, increased thirst, and perhaps a condition of hyperirritability of peripheral nerves. Then appear unrest and fibrillary contractions of various muscles, especially of the tongue; these become more frequent and are accompanied by a stiffness of the extremities and clonic contractions of groups of muscles. The clonic contractions then extend to all the muscles, leading to the typical tetanic attacks, which are accompanied by salivation and increased cardiac and respiratory activity, and a rise of temperature. These attacks are succeeded by a condition of prostration, during which the dyspneic respiration gradually returns to normal. The animal may apparently completely recover, but, within a few hours, or a day or two, new attacks develop and death occurs. The duration of life after complete removal of the parathyroids rarely exceeds ten to fourteen days.

If only two or three parathyroids are removed, there may develop a condition of latent tetany; in this there are often no symptoms except under special conditions. Among the influences provoking attacks of tetany the occurrence of pregnancy or lactation is most prominent, although the administration of various poisons may also provoke an attack.

It is now generally held that the tetany following parathyroidectomy is due to the accumulation in the blood of toxic substances, which in the normal animal are neutralized in some way by the action of an internal secretion of the parathyroids.

MacCallum and Voegtlin suggested that the tetany is due in part to a loss of calcium from the tissues; the injection of calcium salts relieves the symptoms. From later experiments (212) they conclude that the action of calcium in curing the symptoms of tetany is due very largely to its depressing the excitability of the motor nerves. It is interesting to note, in this connection, that Thompson, Leighton and Swarts (see 153), and Morel (147) have found that traumatism of bone prevents tetany from removal of the parathyroids; it does not, however, prevent the development of fatal cachexia.

In some cases of parathyroidectomy nutritional disturbances, leading to death in cachexia, are the most marked or only symptoms (Gley, 74; Thompson and Leighton, 208, 120).

Parathyroid Deficiency in Man.—The clearest cases of parathyroid insufficiency in man are those in which the glands have been more or less completely removed or injured at operations. Cases of this character are

now rare, but occasionally occur (Pool, 174; Branham, 32; Erdheim, 54) as a result of accident, especially, apparently, from an interference with the circulation of the glands (Halsted, 83).

The symptoms of post-operative tetany in man are very similar to those described in animals. If death does not occur in a short time, a chronic condition of latent tetany or of subtetanic hypoparathyreosis (Halsted) develops. Such a condition may continue for years, the patients having attacks of tetany at irregular intervals.

Another form of tetany, in which it is reasonable to suppose that a condition of parathyroid insufficiency exists, is that which occurs in pregnancy or lactation; at other times there may be no evidence of tetany. This form is strikingly like that observed in parathyroidectomized animals; it has also been observed in women after operations on the thyroid (Frank, 66). Krabbel * reports the case of a girl who for seven years had tetany only during menstruation; she was completely relieved by the implantation of parathyroids into the tibia.

Another form of tetany, the etiology of which has been the subject of much discussion, is that of children. A number of writers have reported finding extensive hemorrhages into the parathyroid glands in this condition. Others, however, state that such hemorrhages are comparatively common in infants, and maintain that they are found as frequently in children who do not show tetany symptoms during life as in those who do (Auerbach, 10). Extensive hemorrhages into the parathyroids have been reported in cases of sudden death, with spasms, of children (Grosser and Betke, 78).

Attempts have been made to bring other forms of tetany (that of gastrointestinal origin, toxic tetany, and those forms associated with various nervous diseases) into relation with the parathyroids.

Parathyroid deficiency has been suspected to be a factor in paralysis agitans, myotonia congenita, myoclonia, chorea, osteomalacia, rickets, and eclampsia.

Therapeutic Uses of Parathyroid

Experimental.—Some of the earliest investigators of the physiology of the parathyroids (Lusena, Vassale, Generali, Moussu, MacCallum) found that the tetany could be prevented or checked by the injection (subcutaneous, intraperitoneal, or intravenous) of emulsions of the parathyroids; favorable results were also reported from the feeding of the gland. Berkeley and Beebe (21) found that the active part of the gland is the nucleoprotein fraction; this is efficient when given by the mouth, but much more so when given subcutaneously.

* This author also reports a case of a man with hypoplasia of the genital organs who had tetany (relieved by transplantation).

The treatment of parathyroid tetany by the administration of the glands differs in important particulars from that of myxedema by the administration of thyroid. The effect of thyroid is strictly specific; no other gland, substance, or method will relieve the symptoms. It has been found, on the other hand, that parathyroid tetany can be effectually checked by the administration of salts of calcium, magnesium, strontium, and barium, and, in at least some cases, by the injection of large amounts of sodium chlorid solution.

In most of the experiments in which parathyroid was administered only the symptoms of tetany were relieved, the animals dying later in cachexia; the cases of complete recovery may have been due to the hypertrophy of accessory glands. Thus, valuable as the administration of the gland may be in checking the symptoms of tetany and in prolonging life, it is open to question whether it is possible to obtain permanent cures in complete parathyroidectomy. Its greatest field of usefulness would seem to be in combating the immediate effects of parathyroid deficiency and in prolonging life until injured glands can regenerate or accessory ones hypertrophy.

For the permanent relief of parathyroid insufficiency transplantation of the glands is indicated, but the results have been disappointing (Halsted, 84; Leischner and Köhler, 121; Landois, 118). Halsted concludes that transplantations succeed only when a parathyroid deficiency has been previously induced, and that parathyroid tissue transplanted in excess of what is urgently required by the organism does not live.

Organotherapeutics in Man.—Efforts to control the tetany following removal of the parathyroids, or the effects of interference with their blood supply, by the administration of parathyroids, have met with variable degrees of success. Halsted (83, 84) states that, "in a patient suffering greatly from subtetanic hypoparathyroidism as the result of two operations upon a large goiter, tetany had for three years been averted, and the status parathyreoprivus made endurable by the feeding of parathyroids, by hypodermic injections of the nucleoproteids of the parathyroid gland (Beebe), and for almost one year by the administration of calcium lactate (MacCallum and Voegtlin)." At the beginning six dried beeves' parathyroids were given every three hours; the effect "was almost instantaneous and most marvelous." The dose was then reduced to one gland three times daily; further reduction could not, for several weeks, be borne. Later fresh glands were substituted; these were more readily taken than the dried ones.

Branham (32) used subcutaneous injections of emulsions of beef parathyroids with much success in a case following operation for goiter; the tetany disappeared permanently after the second injection.

Schneider (196) reported a case of post-operative tetany in which the administration of the dry parathyroid of the horse (0.02 gram in

two days) was followed by marked improvement; the symptoms later reappeared, but disappeared after 0.03 gram of parathyroid. Other favorable reports have recently been published by Bircher (26) (two cases) and others.

Several cases have been reported in which relief or cure of post-operative tetany followed transplantation of the gland.

Leischner and Köhler (121) obtained only temporary relief from isotransplantation in one case, and no results in another. They suggest that in some of the apparently successful cases of isotransplantation in man there was a regeneration or recovery of function by the parathyroid tissue of the patient.

Parathyroid has been administered with varying results in a number of other forms of tetany and in other conditions; the possible influence of suggestion can not always be eliminated.

Berkeley relieved the symptoms of *gastric tetany* by the administration, by mouth, of fresh beef parathyroid; Moffitt (146) also reports favorable results from the use of the dried powder, and later from hypodermic injections of the nucleoproteid of beef parathyroids.

Loewenthal and Wiebrecht (126) obtained good results from parathyroid feeding in infantile tetany; others have reported entirely negative results.

Berkeley (20) has secured better results from the administration of parathyroid in *paralysis agitans* than from any other remedy. The treatment should be long continued. Of twenty-six cases treated, five were not benefited, three showed temporary improvement, and eighteen grew progressively better during the whole period of treatment. Roussy and Clunet (188) observed slight temporary improvement in two cases, a distinctly bad effect in two others, and no effect in a fifth case; they report a condition of parathyroid hyperplasia (whether primary or secondary not determined) in this disease. Oppenheim recommends the administration of doses corresponding to 0.05 gram of the fresh gland several times a day.

Favorable results have been reported from the use of parathyroid in eclampsia, epilepsy, and chorea (especially of adults) (Garavini, 72).

Method of Administration

Various commercial dry preparations have been put on the market. Berkeley states that in his experience such preparations have not proved of value, and recommends the use of glands prepared as follows: Freshly obtained ox glands are trimmed, pressed dry between folds of gauze, minced and rubbed up in a mortar with an excess of milk sugar, all the operation being carried out aseptically. One per cent. boric acid is added as a preservative and a trace of a volatile oil, usually peppermint. The

preparation is administered in capsules, each corresponding to one-half grain of the fresh gland. The dose is three to five capsules daily.

Berkeley and Beebe have suggested, especially for hypodermic use, a nucleoprotein prepared from saline extracts of the glands by precipitation with dilute acetic acid. Fifteen minims of the one to one thousand solution of this are given hypodermically several times a day. Care should be taken not to inject it into a vein, owing to the danger of thrombosis.

The administration, both by the mouth and hypodermically, of large doses of parathyroid to human beings (not suffering from tetany) had practically no effect (Esterbrook); there seems, at present, no reason to fear untoward results such as occur in thyroid and suprarenal medication.

THE SUPRARENAL GLANDS

The use of suprarenal glands as organotherapeutic agents in the proper sense of this term, that is, their administration to supplant suprarenal deficiency, has met with but a limited degree of success. The study of these organs has, however, led to the discovery in them of a principle (epinephrin) which has proved of great therapeutic value in many conditions in which the question of suprarenal insufficiency is not involved.

The suprarenal glands of man and the higher animals consist of two parts. The cortex is of mesodermal origin and belongs to a system known as the interrenal system. The medulla is of ectodermal origin, originating as a part of the sympathetic nervous system; it is a part of the "adrenal" or "chromaffine" system (so-called from its affinity for the salts of chromic acid). A very considerable amount of chromaffine tissue is found in man outside of the suprarenals (in small masses along the sympathetic nerve, and in the carotid gland); interrenal tissue is also often found in other parts of the body outside of the suprarenals.

These two parts are, however, for the most part, so intimately connected, anatomically, in man and the higher animals, that it is very difficult to study their functions separately, and most of the knowledge on this subject is based upon observations and experiments upon the entire organ. It may be stated here, however, that it is known that a very important function of the medulla is the production and secretion of epinephrin, a substance necessary to the proper functioning of many parts of the body.

Effects of Disease of the Suprarenal Glands.—The first important contribution to the knowledge of the function of the suprarenals was the classical paper of Addison (1855) on the disease which bears his name. This disease is characterized by a condition of muscular and cardiac weakness, usually with a low blood-pressure, a subnormal temperature,

apathy, disturbances of the digestive tract (vomiting and diarrhea), pigmentation of the skin and mucous membranes, and a progressive cachexia almost always ending in death.

The typical anatomical change found in the suprarenals in Addison's disease is a tuberculous degeneration. The chromaffine tissue in connection with the sympathetic nerve, outside of the suprarenal glands, has also been found involved in a number of cases; in others the chromaffine tissue both in and outside of the suprarenal glands was apparently intact. It is not possible at present to determine whether Addison's disease is due primarily to an involvement of the chromaffine (adrenal) tissue or to that of the interrenal system, or to both.

Absence of epinephrin has been found in a number of cases of Addison's disease (Oliver and Schäfer, 154; Luksch, 131; Ingier and Schmorl).

Recently attention has been called to certain changes in carbohydrate metabolism in this disease which afford further proof of a relation of the suprarenal glands to carbohydrate metabolism; this subject will be discussed later.

Studies of other abnormal conditions of the suprarenal glands in man have only been suggestive of possible functions of these organs. It has long been known that in many cases of congenital malformations (anencephaly, hydrocephalus) the suprarenals show a condition of hypoplasia or of aplasia; in some of these cases only the medulla was involved, the cortex being normal. The relations of these conditions, whether causal or not, have not been definitely determined. On the other hand, excessive growth has been reported in cases of tumors of the suprarenals.

Hypoplasia of the suprarenals has been met in a few cases of retarded sexual development, and in cases of osteomalacia and status lymphaticus. On the other hand, hypernephromas originating from cortical suprarenal tissue have in a number of cases, in infants and young children, been associated with sexual precocity; this observation suggests a relation between the suprarenals and the sex organs.

Many attempts have been made to correlate certain conditions of high blood-pressure with hypertrophy of the suprarenals, especially of the medulla; but it is not certain that the suprarenal changes are primary.

Extirpation of the Suprarenals in Animals.—The removal or destruction of both suprarenals leads to death within a few hours or days; exceptions to this rule are due to the presence of accessory glands. Biedl describes the effects as follows: for one to two days the animals seem to be entirely normal; on the second or third day there is a loss of appetite; afterward apathy and muscular weakness become apparent; the movements become stiff and uncertain. Then great prostration follows, the animal is unable to rise, and lies extended on its abdomen. There is a marked fall of temperature (to 30° C. or under), respiration is labored,

the heart is irregular and weak; the animal usually dies (in three to six days) in this condition of paralysis. Occasionally there are muscular twitchings, more rarely convulsions.

Experiments on animals deprived of their suprarenals have revealed interesting relations of these glands to carbohydrate metabolism. Bierry and Malloisel (24) and Porges (175, 176) have found a condition of hypoglycemia; Porges found the same in three cases of Addison's disease (see also 22).

The reduced amount of sugar in the blood has been held to explain, in part, the most striking symptom following the removal of the suprarenals—the asthenia; favorable results in Addison's disease are reported from the administration of sugar (Pitres and Gautrelet, 172).

Animals deprived of their suprarenals are easily fatigued; if forced to exercise, they may die suddenly.

Such experiments as the above show that the suprarenals are organs essential to life, and also give some indications as to some of their functions.

The questions as to which part of the suprarenal system, the interrenal (cortical) or the adrenal (medullary), or whether both are essential to life, has been much debated; some authors have considered that only the former, others that only the latter, is essential to life. The tendency perhaps has been to consider the medulla (the epinephrin-containing part) the vital portion of the gland. Biedl, without denying that the adrenal (chromaffine) tissue may be essential to life, holds that it has been demonstrated that the interrenal part is indispensable.

Effect of the Administration of Suprarenal Gland: Epinephrin.—Oliver and Schäfer (154) made the very important discovery that extracts of the medulla of the suprarenal glands, when injected intravenously, cause a marked rise of blood-pressure.

The chemical work of Abel, von Fürth, Takamine, Aldrich, Dakin, Stolz, and others resulted in the isolation and, later, synthesis of a definite chemical compound, named by Abel epinephrin, by Takamine adrenalin. Chemically this compound is dioxyphenylethylolmethylamin ($C_9H_{13}NO_3$). It is levorotatory. The compound made synthetically is optically inactive, and has only about one-half the physiological activity of the natural compound (Cushny, 46; Schultz, 197); it can, however, be separated into two optically active isomers, one of which, the levo-compound, is identical in every respect with the natural base.

Physiological Action of Epinephrin.—Knowledge of the details of the physiological action of epinephrin has increased greatly within the last few years, and it is now possible to bring nearly all of the facts accumulated (more especially by Langley, Elliott, Brodie and Dixon, and Dale) together and express them in the form of a general law: The effects of epinephrin are everywhere essentially the same as those of the stimulation

of the sympathetic nerves. The action is peripheral, and upon what is known as the "myoneural junction," which is a part of the "receptive substance" (Langley) of the cell.

The following illustrations show some of the applications of this law:

Blood-Vessels.—It has been known for some time that the very great rise of blood-pressure following the intravenous injection of epinephrin is due largely to a peripheral constriction of the blood-vessels, especially of those of the splanchnic area. The vasoconstrictor muscles of the blood-vessels are innervated by the sympathetic nervous system. In organs (heart, lungs, brain) in which the sympathetic vasoconstrictor innervation is but slightly developed (or, according to some writers, absent) epinephrin has little (according to some, no) vasoconstricting effect.

Meltzer and others pointed out that epinephrin may cause a vasodilatation in certain cases, and recently Dale has brought forward further evidence that there is a sympathetic vasodilator (inhibitory) innervation of certain vessels; these dilate under the influence of epinephrin and of the stimulation of the sympathetic nerves if the effects of the constrictor fibers are excluded by the action of ergotoxin.

In this connection it may be remarked that the effect of epinephrin upon the blood-pressure of animals constitutes a useful method for determining the relative strength of different preparations of this drug; its effect upon isolated arteries is a very delicate method of detecting its presence (Meyer's method).

The vasoconstricting action of the drug is seen when it is applied to a mucous membrane or to the abraded and bleeding skin; the structures become blanched and hemorrhages from small vessels cease.

Heart.—Extracts of suprarenal and epinephrin cause a marked acceleration and strengthening of the heart beat; the effects are the same as those of the stimulation of the accelerators (sympathetic motor nerves). The maximum rate reached is the same as the maximum rate after stimulation of the accelerators; this rate may be maintained for some time by the repeated injections of small doses (Hunt, 97).

In the intact animal the acceleration of the heart is frequently (almost always, if the dose is large) prevented, at least at first, by a simultaneous stimulation of the vagus centers; the latter is attributed largely to the high blood-pressure.

Alimentary Tract.—The effect of epinephrin on the alimentary tract is throughout the same as that of the stimulation of the sympathetic nerves. When the latter cause inhibition, epinephrin does also; when the stimulation of the sympathetic causes contraction, epinephrin does the same. Thus, in the rabbit epinephrin causes relaxation of the entire alimentary tract, with the exception of the pyloric, ileocecal, and internal anal sphincters, which contract under its influence. The innervation

of the alimentary tract varies in different species of animals; the effects of epinephrin vary in a corresponding manner.

Cannon and de la Paz (35) believe that the inhibition of the intestinal movements which results from strong emotions is due, at least in part, to increased secretion of epinephrin; they have shown the latter to occur during fright.

Cannon and de la Paz suggested the use of strips of the intestine as a very delicate test for the presence of epinephrin, especially in blood.

Urinary Bladder.—The same relations hold for the bladder as for the alimentary tract; in those animals in which stimulation of the sympathetic causes relaxation of the bladder and contractions of the urethra, epinephrin does the same; when stimulation of the sympathetic is without effect upon the bladder, epinephrin is also without effect.

Uterus.—The effect of epinephrin upon the uterus is determined by the character of the sympathetic innervation. It, like the stimulation of the sympathetic, causes powerful contractions of the pregnant uterus and of the non-pregnant uterus in certain animals. In the virginal uterus of the cat, however, both epinephrin and stimulation of the sympathetic cause relaxation. Dale was able to demonstrate the presence of a sympathetic inhibitory supply to the uterus of other animals also. After very large doses of ergot, which paralyze the motor nerves, stimulation of the sympathetic or the administration of epinephrin causes relaxation of the uterus in all cases. The conditions are analogous to those which hold for certain blood-vessels.

The action of epinephrin upon the uterus is one of the most delicate tests for the drug ("Fränkel's test"); a solution containing one part in twenty millions is active.

Bronchial Muscles.—The effect of epinephrin upon the bronchial muscles is of special interest, since it is claimed that attacks of bronchial asthma in man may be relieved by it. This suggests the presence of sympathetic inhibitory nerves to the bronchial muscles, but attempts to demonstrate their existence have been unsuccessful. Similarly, efforts to demonstrate an action of epinephrin upon the bronchial muscles have usually failed. Eppinger and Hess, however, believe that epinephrin may, through the stimulation of sympathetic inhibitory nerves, counteract the contractions of the bronchial muscles caused by increased vagus tonus. Januschke and Pollak found it to relax the bronchial muscles in muscarin asthma and to have some relaxing effect in normal animals.

Action on the Eye.—The intravenous injection of epinephrin into animals causes the same changes in the eye as follow the stimulation of the cervical sympathetic nerve, viz., retraction of the nictitating membrane and of the eyelids, protrusion of the eyeball, and dilatation of the pupil (through stimulation of the dilator muscle). Instillation of epinephrin into the eye is far more effective in causing dilatation of the

pupil if the superior cervical ganglion has been extirpated than it is in normal animals (Meltzer and Auer); this reaction has been utilized in locating the site of injuries to the sympathetic (Cords, 39; Sébileau and Lemaitre, 198). Solutions of epinephrin applied repeatedly to the normal human eye cause dilatation of the pupil (Schultz, Wessley). Slight lesions of the cornea greatly facilitate the reaction; Cords (40) has used the reaction to detect erosions and ulcers of the cornea.

The pupil is said to be abnormally sensitive in some cases of diabetes mellitus and of Graves' disease (Loewi's reaction).

Loewi considered this increased sensitiveness of the pupil to epinephrin in Graves' disease to be due to an increased irritability of the sympathetic nerves caused by the condition of hyperthyroidism.

The pupil of the frog's eye (either *in situ* or enucleated) dilates upon the application of very minute amounts of epinephrin; Meltzer and Auer suggested that this reaction might be used for the detection and estimation of this substance. The reaction was elaborated by Ehrmann, and has been frequently used in the study of various problems connected with the suprarenal glands; it has, however, a number of limitations which have not always received sufficient consideration at the hands of some investigators.

Metabolism.—Epinephrin has little effect upon nitrogen metabolism except in inanition, when it causes a considerable increase in protein metabolism; this effect is attributed by Eppinger, Falta, and Rudinger to a stimulating action upon the thyroid.

Epinephrin has a marked effect upon carbohydrate metabolism; this is thought to result from a stimulation of certain sympathetic nerves. The glycosuria is accompanied and caused by a hyperglycemia and by a diminution of or disappearance of glycogen from liver and muscle. The degree of glycosuria is largely determined by the amount of glycogen in the liver, although some excretion of sugar is caused in starving animals.

Zuelzer, Embden, and others have found that, when epinephrin is added to blood used in perfusing an excised liver, it causes the latter to liberate sugar into the hepatic vein in far greater amounts than when normal blood is used.

The above facts lead to the conclusion that the action of epinephrin in producing glycosuria is due to a setting free or mobilization of sugar stored as glycogen; the pancreas is believed to inhibit this action. Several recent writers (Underhill and Closson, 210; Macleod, 135; Frank and Isaac, 64) have attributed epinephrin glycosuria to the effect of stimulation of the sympathetic nerves going to the liver; this would bring the action in line with the other effects of epinephrin.

Epinephrin glycosuria is more pronounced in animals deprived of their pancreas; it is not easily produced in Addison's disease, unless glucose is given at the same time (Pollak, 173).

It is now generally held that epinephrin has an effect upon the "sugar tonus" similar to that upon the vasomotor tonus, and that this effect is exerted through the sympathetic nerves to the liver.

According to Eppinger, Falta, and Rüdinger, the thyroid has an intensifying effect upon the action of epinephrin.

Functions of the Suprarenals.—It has been conclusively shown that the suprarenals are glands essential to life; it has also been shown that both parts of the gland (the adrenal or medullary, and the interrenal or cortical) are important, although it can not be stated that one is more important than the other.

Experiments show that the suprarenal glands continuously secrete into the blood epinephrin, a substance which, as was shown above, has a stimulating action upon the organs innervated by the sympathetic nervous system. The physiological tonicity of these organs is maintained in this way, and a normal blood-pressure, a normal heart rate, etc., are insured. The experiments on the extirpation of the glands and on the administration of epinephrin show that their normal functioning is essential to the maintenance of the normal sugar tonus of the blood, which is essential for muscular activity; this effect also is probably exerted through the sympathetic nervous system.

Thus, there can be no doubt that an extremely important function of the suprarenal glands is the secretion of epinephrin. This function is exerted entirely by the medullary portion of the gland; the same function is also performed by the chromaffine tissue in other parts of the body. It has been possible to determine, within rather wide limits, the amount of epinephrin secreted daily in animals; Biedl calculates this to be about 0.00432 gram for a dog of fifteen kilograms; only about one-fortieth of this amount is found in the blood at any one time, showing that there is a continual production and consumption of the substance. The normal gland contains from 0.1 to 0.17 per cent. of epinephrin, or a total of about 4.5 mgr.

Whether the suprarenal medulla has functions other than the production of epinephrin has not been determined.

Much less is known as to the function of the suprarenal cortex and other parts of the interrenal system. That this system is essential to life is shown by the results of its removal. The fact that it, like the adrenal tissue, is found in all classes of vertebrates is an indication of its importance, as is the further fact that removal of part of it leads to compensatory hypertrophy of the remaining parts.

Many facts indicate that there is some relation between the suprarenal, especially the cortex, and growth and the functions of the sex cells, but the nature of the relation is obscure. Several writers, for example, have stated that the cortex hypertrophies after castration (Schenk, 195).

Marchand described a hypertrophy of the suprarenals with atrophy of the ovaries in pseudohermaphroditism. An association between tumors of the suprarenals and precocious sexuality has been found (Wooley; Glynn; Bullock and Sequeira, 33; Alezais and Peyron, 4); the fact that this condition occurred with tumors of cortical, but not with those of medullary, origin suggests that the former part has some relation to the sex organs. On the other hand, it is stated that in Addison's disease and in congenital hypoplasia of the suprarenals there are marked changes in the testicles.

Efforts have been made to obtain further knowledge of the functions of the cortex by means of histological and chemical studies. The most characteristic feature of the cortex is its content of doubly refracting, lipoid substances; among these lecithin and certain esters of cholesterin are especially abundant.

Hunt (98, 99) isolated cholin from the suprarenals. Later Lohmann (128) showed that about nine times as much of this substance could be obtained from the cortex as from the medulla. Some investigators have attached considerable significance to this discovery of cholin, but it seems to have none beyond indicating the presence in the suprarenals of a considerable amount of lecithin or lecithin-like substances from which cholin is easily obtained.

The hypothesis has been suggested that one of the functions of the suprarenal cortex is to make and secrete lipoids for use in other parts of the body (Albrecht and Weltmann, 3); there is not much evidence to support this suggestion.

Another theory which has, in one form or another, long been prominent is that the suprarenal glands, and especially the cortical portion, neutralize various poisons formed either within the body or introduced into it from without. On the whole, however, the theory that the cortex secretes a hormone having an important effect upon processes of growth and development is more plausible; this hypothesis is supported by the observation of changes in the cells very suggestive of secretory activity.

Therapeutic Uses of the Suprarenal Gland and of Epinephrin

Organotherapeutics—Experimental.—Efforts to overcome the effects of the removal of the suprarenals in animals have been made both by the administration of the gland or its extracts, and by transplantation. Neither has met with much success. In no case was life prolonged for more than a few hours after the administration of the gland to animals from whom the suprarenals had been removed. Considerable improvement in the symptoms (increase of blood-pressure, improved respiration) have frequently been reported from the subcutaneous or intravenous injection of

extracts of the gland, but the results did not differ from those observed in animals near death from poisons and other causes.

So far transplantation of the suprarenals has been successful only as a preventive measure; that is, it was possible to prevent the characteristic effects of the removal of the glands by the previous transplantation of a gland. Apparently, when the effects of the removal of the glands had become manifest, it was not possible to delay death by the transplantation of the glands of other animals.

ORGANOTHERAPEUTICS IN SUPRARENAL DEFICIENCY IN MAN.—*Addison's Disease.*—Addison's disease is the only condition in man in which a suprarenal insufficiency clearly exists, and most of the interest in the organotherapeutic use of the suprarenal centers around it.

For the use of suprarenal preparations in Addison's disease, see Vol. III, Sec. IV, Chapter V. (See also references 2, 29, 34, 52, 73, 79, 108, 204, 223.)

Other Conditions of Suprarenal Insufficiency.—Suprarenal gland and epinephrin have been administered in a number of conditions in which an insufficiency of the glands had, upon inconclusive evidence, been supposed to be present; the results have been inconclusive.

It has been supposed, for example, that a condition of suprarenal insufficiency exists in many chronic diseases, especially tuberculosis, and the administration of the gland, or of epinephrin, recommended accordingly; Boinet has been especially prominent in the advocacy of this form of treatment. It has also been recommended in certain forms of neurasthenia associated with low blood-pressure. It has found a more extensive use in the cardiovascular exhaustion of acute infectious diseases. In this condition, however, it is used as are other cardiovascular tonics, i. e., it is used as are other drugs, and not as an organotherapeutic agent in the usual meaning of this term.

The suprarenal gland, and especially epinephrin, has been used extensively in *osteomalacia.* The views as to the value of this mode of treatment (proposed by Bossi) are conflicting; many report favorable results. Novak (151), for example, reports seven cases treated by subcutaneous injections of 0.5 to 1 c. c. of the one to one thousand solution; three were improved, in two there was a slight diminution of the bone pains at the beginning, and in two there was no effect. He believes that it should be tried in all cases, and states that no bad effects have been observed, except sometimes slight dizziness and palpitation.

Attempts to deduce a rational basis for the use of suprarenal in osteomalacia have been made from the following facts: There seems to be an antagonistic (or supplementary) relation between the ovaries and the suprarenals; the latter hypertrophy when the former are removed or are atrophic, and also in pregnancy when parts of the ovary are physiologically quiescent. Christofoletti (37) has advanced the hypothesis that

in osteomalacia there is a hypofunctioning of the chromaffine tissue due to a hyperfunctioning of the ovaries. As was pointed out above, however, in discussing the relation between the suprarenals and the sex glands, the cortex seems to be the part of the former which is chiefly involved, whereas, in the treatment of osteomalacia, a product of the medulla (epinephrin) is usually employed. At present the favorable results which seem to follow, at least at times, the use of epinephrin in osteomalacia can not be satisfactorily explained.

Certain writers have drawn analogies between the pigmentation, the lassitude, and the vomiting of pregnancy, and some of the symptoms of Addison's disease, and have treated some cases of *vomiting* of *pregnancy* by the administration, *per os* or subcutaneously, of ten drops of the one to one thousand solution of epinephrin; benefit has been reported from such treatment. Epinephrin, when injected intravenously, inhibits the movements of the stomach; possibly it may do the same in pathological conditions from subcutaneous administration.

Eppinger and K. H. von Noorden (53) found that the severe diarrhea produced in dogs by the feeding or injection of thyroid could be checked by the administration of epinephrin. They also report that excellent results were obtained in three cases in the *diarrhea of Graves' disease* from clysmata containing thirty drops of the one to one thousand solution of epinephrin in three hundred c. c. of water. They believe that the diarrhea in this condition is due to a stimulation of the vagus nerves, and that this is counteracted by the effect of the epinephrin upon the inhibitory sympathetic nerves. The treatment was successful in the diarrhea of one case of Addison's disease, and they suggest that it may be useful in other forms of nervous diarrhea.

Other Uses of Suprarenal.—The suprarenal glands and their preparations are used more extensively for the control of *hemorrhage,* and as a *cardiovascular stimulant,* than for any other purpose; solutions of the active principle (epinephrin) have largely replaced the crude extracts of the glands for this purpose. The use of the drug in these cases does not differ from that of other pharmacodynamic agents, and its detailed consideration does not properly belong in a chapter on organotherapeutics. The action of the alkaloid, epinephrin, has, however, certain peculiarities which may properly be pointed out in this connection. When applied locally it causes an intense constriction of blood-vessels, and this action largely prevents its absorption; hence, when given by the mouth or subcutaneously, it produces systemic effects only after *very large doses.* One hundred times as much is said to be required to produce an effect when given subcutaneously as when given intravenously. Intramuscular injections are much more efficacious than subcutaneous ones.

Epinephrin also differs from most alkaloids (Straub, 201) in that it does not accumulate in the tissues and that it is quickly destroyed in

the body; it exerts its action only during its passage into the tissues, and hence its action depends upon the difference in the concentration in the tissues and the concentration in the blood, rather than upon its absolute amount. Moreover, its effect does not become less after repeated administration; the hundredth injection, for example, was found to cause as great a rise of blood-pressure as did the first and subsequent injections.

The above considerations indicate that the best results, when the drug is used as a cardiovascular stimulant, are to be expected from the continuous infusion of a weak solution. This conclusion coincides with clinical experience. Although life has undoubtedly been saved by intramuscular or intravenous injections of comparatively strong solutions (four minims of the one to one thousand solution, for example), the best results have been obtained by the continuous infusion of a solution of one to fifty thousand or one hundred thousand in normal saline solution.

The use of this drug as a cardiovascular stimulant (Crile) has proved especially valuable in conditions of *cardiac* and *vasomotor failure* under anesthesia (general and spinal), in shock and acute hemorrhage, and in cases of poisoning, as by chloroform and chloral, although very favorable results have also been reported in the low blood-pressure of pneumonia and other acute infectious diseases, especially of children. In diphtheria it is said to relieve prostration and asthenia, aside from its effect on blood-pressure. [It is valuable in all conditions in which there is vasomotor paralysis.—Editor.] Rolleston (185) administered it by the mouth in ten-minim doses of the one to one thousand solution every two to four hours, according to the severity of the attack. Especial emphasis has recently been placed upon its value in *peritonitis*. Thus Heidenhain (90) and Holzbach (94) recommend its administration by continuous infusion previous to operation; they state that a high blood-pressure may be maintained in this manner for hours. Heidenhain concludes that if, as a result of the infusion, the blood-pressure is raised, and the cyanosis and coldness of the extremities disappear, an operation is permissible; otherwise nothing is of avail. Heidenhain states that the intravenous injection of the undiluted solution, one to one thousand, is not without danger; he considers eight drops (0.5 c. c.) of the one to one thousand solution per liter normal saline solution sufficient.

Laewen and Sievers (117) state that in certain conditions of stoppage of the heart the injection of 0.2 c. c. of the one to one thousand solution directly into the heart is permissible.

The greatest field of usefulness of epinephrin, however, is as a *local hemostatic*.

It is used to check epistaxis, and also hemorrhages into the rectum (as from hemorrhoids), bladder (one hundred c. c. of the one to ten thousand solution, for example), uterus, etc., and to relieve congestion of the

conjunctiva and of the mucous membranes of the nose (as in rhinitis and hay fever), and of other organs.

It has been used in *post-partum* hemorrhage; it not only constricts the blood-vessels, but causes a contraction of the muscle fibers of the uterus.

It may be applied in solutions of from one to one thousand, to one to twenty thousand, either directly or on cotton, or as a spray, or in ointments; cavities, such as those of the nose and uterus, may be packed with gauze wet with a solution one to five thousand or one to ten thousand.

It has also been administered by the mouth (ten to twenty drops of the one to one thousand solution) and also subcutaneously, in gastric and intestinal hemorrhages (as in typhoid fever), although some report but little benefit from such use (Jacobson, 105).

Epinephrin has been extensively used to enhance the action of local anesthetics, such as cocain, novocain, etc. It exerts this action not only by delaying the absorption of the anesthetic (by which the danger of systemic intoxication is also lessened), but, in the case of some of the drugs of this class, it seems to have a direct effect upon the action of the anesthetic itself (Esch, 55). On the other hand, it is stated (Fröhlich and Loewi, 69) that cocain increases the sensitiveness of various organs (blood-vessels, urinary bladder, eye) to epinephrin (and to direct stimulation of the sympathetic nerves), so that a weaker solution of epinephrin suffices to cause constriction of vessels when combined with cocain. Such combinations of epinephrin and cocain are useful, not only in cases of operation, but in examinations.

A few drops of epinephrin solution, one to one thousand, are frequently added to Schleich's solutions for local anesthesia; it is also used in connection with the induction of spinal anesthesia.

Epinephrin has been much used to relieve the attacks of *bronchial asthma;* it is applied locally as a spray (epinephrin one part, water seven hundred and fifty parts, glycerin two hundred and fifty parts (Zuelzer, 236); aqueous solution, one to one thousand, to one to four thousand), or as an ointment (thirty to sixty drops of the one to one thousand solution in *adeps lannæ hydrosus* and *petrolatum,* one dram each), by subcutaneous injection or by rectal suppository (Matthews, 141).

Clinicians hold widely divergent views as to the value of epinephrin in *pulmonary hemorrhage;* some consider it of much value, whereas others consider it contraindicated (229). Attention was called to the fact that experiments on animals showed that epinephrin has little if any constricting action upon the pulmonary vessels. Wiggers (227) found that the outflow from the pulmonary vessels was decidedly increased by epinephrin; he considers this due to the distention of these vessels by the augmented contraction of the right ventricle.

The blood-vessels of the kidneys and of the intestines are said to be especially sensitive to epinephrin; Wiggers found renal (228) and, un-

der certain conditions, intestinal hemorrhages (226) to be quickly checked by the intravenous or intramuscular injection of the drug.

It is stated that it has been used with marked success in hemophilia (Lange, 119).

Preparation and Dosage

These subjects have been discussed above; a few further points may be considered.

The dried powder (*Glandulæ suprarenales siccæ* U. S. P.) is used chiefly for oral administration; the average dose is four grains. Before the isolation of epinephrin the dried gland was used for the preparation of extracts. Such extracts are efficient, and are far less expensive than the commercial solutions. Among the drawbacks to their use, however, is the fact that they make excellent culture media for bacteria, and it is said that tampons wet with such solutions readily cause infection when left in the nose and other cavities. It has also been shown recently that the commercial preparations of the dry gland vary greatly in activity; Hale and Seidell (82) found some samples to be seven times as active as others.

At present the drug is employed almost exclusively in the form of solutions of one of the salts, usually the chlorid, of epinephrin. The solutions on the market are usually one to one thousand in normal saline solution; they usually contain a preservative. They deteriorate rather rapidly on exposure to air and light, becoming first reddish and then brown; slightly reddish solutions may be used, but the brown ones should not be used. Many of the commercial solutions as found on the market vary greatly in strength (Schultz, 197); this may be due to deterioration through age, or the solutions may not have been made of proper strength originally. They should be physiologically standardized, unless a very pure preparation of the active principle is used.

The active principle is known by a great variety of names: adrenalin, adrenin, adnephrin, adrin, suprarenalin, supracapsulin, hemisin, suprarenin (both natural and synthetic), epirenan, etc. Most of these names are proprietary. It seems better to use the word epinephrin, proposed by Abel, to designate the active principle; the English use the similarly unprotected name adrenin.

Untoward Effects

Considering the extent to which the drug is used, accidents are very rare. A few deaths have been reported from the injection of the one to one thousand solution into veins or into the uterus (Braun; Heidenhain, 90). One milligram injected into a vein has caused alarming symp-

toms; 0.3 mg. applied to the uterus has caused collapse for one-half hour (Müller).

The intravenous injection of epinephrin is contraindicated in organic heart lesions, nephritis, and arteriosclerosis (Kauert, 106).

A number of cases of necrosis and gangrene of the skin have been reported following the subcutanous injection; these occurred for the most part in the aged. Necrosis of the jaw has also been reported.

Severe hemorrhage following its local application has been described; this was attributed to the use of too strong solutions, which constricted larger vessels, so that the surgeon neglected to tie them.

Its repeated administration to animals causes necrotic changes in the arteries; very large doses cause fatal pulmonary edema.

THE HYPOPHYSIS

It is only within very recent years that knowledge of the functions of the hypophysis and of its derangements has approached a point where it is possible to speak of a rational organotherapeutics in connection with this gland. Our knowledge of conditions of deficient functioning of the hypophysis, in which alone a true organotherapeutics would be indicated, is still very imperfect, and the gland has not been used extensively in these. On the other hand, recent studies have shown that a part of the hypophysis contains a substance which, like epinephrin, has marked pharmacodynamic effects, and which promises to be of therapeutic value, not as an organotherapeutic agent, but in the way that epinephrin and other drugs are of value.

Functions of the Hypophysis.—The hypophysis consists of two principal parts. The larger, anterior lobe, or the epithelial or glandular part (the *glandula pituitaria* proper), is, according to most investigators, of ectodermal origin, arising from the epithelium of the roof of the mouth. The smaller, posterior, or infundibular lobe (the *pars nervosa,* neurohypophysis, or hypophysis proper) arises as an outgrowth of the floor of the third ventricle, and consists largely of neuroglia. Between these lobes, and extending over and into the posterior lobe, is the *pars intermedia,* consisting of epithelial cells and neuroglia and containing colloid. The infundibulum connects the posterior lobe with the third ventricle.

The most important steps in the development of the knowledge of the functions of the hypophysis were the following: The observation of Rogowitsch (1889) that extirpation of the thyroid leads to a hypertrophy of the hypophysis; the discovery of Marie (1889) of an association between acromegaly and anatomical changes in the hypophysis; the discovery of Oliver and Schäfer (1895) that extracts of the gland have marked effects upon the blood-pressure and heart, and the later discovery of Howell (1898) that these effects are due to substances contained in

the posterior lobe; the discovery of Fröhlich (1901) of a relation between the hypophysis and the condition known as *dystrophia adiposogenitalis;* the demonstration (by several investigators, but especially by Paulesco, 1907, and Cushing, 1909) that the total extirpation of the gland is rapidly followed by death, whereas the partial extirpation is followed by very characteristic effects upon growth and development, and the studies of Cushing and coworkers, and of others, upon the relation of the hypophysis to carbohydrate metabolism (1911).

A more detailed study of some of these investigations will serve to show the present state of knowledge of the function of this gland, and the conditions in which it or its extracts may be expected to be of therapeutic value.

Effects of Hyperactivity of the Hypophysis.—For some time after the discovery of a relation between acromegaly and the hypophysis there was much discussion as to whether the disease was due to a condition of hyperactivity (as suggested by Woods-Hutchinson in 1894), or of hypoactivity of the gland. It is now recognized that the former is the case, at least in the early stages of the disease. The primary pathological condition in acromegaly is usually one of simple hyperplasia of the anterior lobe; it frequently shows indications of malignancy. At the same time there seems to be at least a functional involvement of the posterior lobe. In late stages there may be an extensive degeneration of the gland; this has an important bearing upon the therapeutic use of the gland in acromegaly. The marked and almost immediate amelioration which often follows the removal of part of the hypophysis in acromegaly affords proof that the condition is one of hyperpituitarism.

Two sets of symptoms are caused by hypertrophy of the hypophysis: (1) those which are due to the specific hyperactivity of the gland, and (2) those produced by the pressure of a tumor in this region. The specific effects of hyperactivity, which may throw some light upon the normal function of the gland, are marked and characteristic changes in the features and in the extremities, due partly to the growth of the soft tissues, partly to an enlargement of parts of the bones of the head, feet, and hands.

Keith (107) has recently studied in detail the changes in the skull in acromegaly, and the manner in which they are induced. He concludes that an internal secretion of the hypophysis sensitizes tissues, so that they respond to the natural stimuli of growth (mechanical activity and muscular movement) with increased energy. The enlargement of the extremities is due largely to connective tissue growth.

Among other symptoms of acromegaly are lassitude, muscle pains, apathy, and disturbances in sexual activity; there is usually amenorrhea in women and frequently impotence in men. Vasomotor changes in the skin are frequent. Polyuria, with or without glycosuria, is common.

Borchardt (30) found glycosuria in 40.3 per cent. of 176 cases. In later stages, where the hyperactivity of the gland is being replaced by hypoactivity, there is, according to Goetsch, Cushing, and Jacobson (75), not only no glycosuria, but an increased tolerance for carbohydrates; these authors consider both the glycosuria (lowered carbohydrate assimilation) and the subsequent increased carbohydrate tolerance to be due to hyper- and hypoactivity, respectively, of the posterior lobe.

Thus, studies of acromegaly show that there is a close relation between the hypophysis and growth, especially of connective tissue, cartilage, and bone, and also between this gland and carbohydrate metabolism and the activity of the sex glands.

The relation between the hypophysis and growth has been further emphasized by studies on gigantism; in this condition also hyperplastic conditions of the hypophysis are almost invariably found. In many of these cases, however, other glands of internal secretion are so greatly involved that it is impossible to determine whether the changes in the hypophysis are primary or secondary. The other glands chiefly involved are the sex glands, which are markedly atrophic, and the thyroid.

It is interesting to note in this connection that favorable results in precocious gigantism have been reported from the administration of ovary (Maisonave; Hudovernig and Popevicz, 96), and that the changes in the hypophysis in animals which follow castration may be partially prevented by the injection of testicular extracts (Fichera, 58).

In certain cases of dwarfism, on the other hand, the anterior lobe of the hypophysis is said to be destroyed (Aschner, 9).

A condition of hyperpituitarism is believed to exist, as has already been indicated, after castration (which leads to an enlargement of the hypophysis), and also during pregnancy, when some of the functions of the ovaries are in abeyance. There are not only characteristic changes in the hypophysis during pregnancy (Marek; Mayer, 142) (as indicated by a constant and marked increase in size and by very definite histological changes), but certain general symptoms of pregnancy (enlargement of the hands, changes in the facies suggestive of acromegaly) are considered to be due to the hyperpituitarism.

Removal of the thyroid also leads to hypertrophy of the hypophysis. The latter is also found in many cases of hypothyroidism in man; symptoms referable to the hypophysis have been reported after thyroidectomies.

Hypopituitarism.—The condition of hypopituitarism is of more interest in connection with the organotherapeutic use of the hypophysis. This condition is known both clinically and experimentally.

Clinically, a condition of hypopituitarism is known in the disease *dystrophia adiposogenitalis,* first described by Fröhlich (70) in 1901. In this condition there are usually symptoms of a hypophyseal tumor combined with obesity, a hypoplastic condition of the sex glands, and re-

tarded growth or infantilism. Some of these symptoms, notably the obesity, occur also in the later stages of acromegaly.

The view that this condition is really due to a primary involvement (hypofunctioning) of the hypophysis is largely based upon recent experiments on animals, in which the hypophysis was partially removed. Crowe, Cushing and Homans (44, 45) found in such experiments adiposity, polyuria, and transitory glycosuria, loss of hair, subnormal temperature, diminution of sexual activity, and atrophy of the testicles and ovaries; there was a reversion to the infantile type. Histological changes were apparent in the thyroid. These results have been confirmed by Biedl (23), Aschner (8), Livon (124), and others. When operations were performed upon young animals there was a marked retardation of growth and a retention of infantile characters. It is not possible to determine at present whether some of these effects are primary or are secondary to the changes in the sex glands.

Aschner found that dogs recovering from a (partial) hypophysectomy showed a diminished glycosuria reaction to epinephrin, and an increase in carbohydrate tolerance.

Cushing and his coworkers at first believed that the above results were due to removal of part of the anterior lobe; now (75) they believe that some of them (the adiposity and increased carbohydrate tolerance) are chiefly due to removal or injury of the posterior lobe. They believe that there are many cases of hypopituitarism in man, due to obstructive agencies (tumors or hydrocephalus), the existence of which may be discovered by a determination of carbohydrate tolerance.

Several cases have been reported in which the administration of extracts of the hypophysis has caused improvement in the condition of *dystrophia adiposogenitalis*—thus affording additional evidence that this condition is one of hypopituitarism.

In this connection reference may also be made to the effects of the total extirpation of the hypophysis in animals. Although a number of earlier investigators had succeeded in removing the hypophysis and had described the symptoms following such an operation, the most convincing experiments are those of Paulesco and other recent investigators (44, 166, 181). These show that animals deprived of their hypophyses live but a short time (one to three or four days), dying without any very definite symptoms beyond a fall of temperature, tremors, slowed respiration, and a condition of lethargy and coma; before death the temperature may fall to 20° C. or lower. Young animals survive the operation for longer periods (ten days to three weeks).

Destruction of the anterior lobe alone, or of the cortical substance of this lobe, or frequently section of the infundibulum, similarly led to death within a very short time. After removal of the posterior lobe, on the other hand, the animals lived for months or years; there was at first

a lowered tolerance for carbohydrates, or temporary glycosuria, followed by a marked increase in the carbohydrate tolerance.

These experiments showed that the anterior lobe of the hypophysis is a structure essential to life, although they throw but little light on the nature of the action of the gland.

Cushing was able to prolong the lives of animals after total hypophysectomy by the transplantation of the anterior lobe or by the injection of extracts of it, and likewise to tide over periods of threatened cachexia hypophyseopriva in animals retaining anterior lobe fragments which might be physiologically insufficient.

Physiological Effects of Extracts of the Hypophysis.—It was stated above that Cushing was able to prolong the life of animals deprived of their hypophyses by the injection of extracts of the anterior lobes. He found a rise of temperature of 2 to 4° C. in such animals after the injection of the extracts. Administered or injected into normal animals such extracts seem to have no specific effects. Feeding of the anterior lobe seems to cause slightly increased growth in young animals. Exner (56) reported increased growth from the transplantation of hypophyses into young rats; the glands were absorbed.

Oliver and Schäfer found extracts of the entire gland to have pronounced effects upon the blood-pressure. Howell (95) stated that these effects were due entirely to the posterior lobe. Schäfer and Herring, and Herring, and Cushing and Goetsch have found that the active principle seems to be formed in the *pars intermedia*, from which it passes through the posterior lobe and the infundibulum into the third ventricle. There is evidence that the secretion of the posterior lobe is increased after thyroidectomy.

The most marked physiological action of extracts of the posterior lobe is to cause a constriction of smooth muscle and the production of diuresis; it is not certain that the latter is not also due in reality to an action on the smooth muscle of the blood-vessels. These extracts also have marked effects upon carbohydrate metabolism. The constriction of the arteries following the administration of such extracts leads to a marked, and, as compared with the effect of epinephrin, long-continued, rise of blood-pressure. The extracts also cause dilatation of the frog's pupil, strong contractions of the uterus, and glycosuria, or lowered carbohydrate tolerance. There is thus a resemblance between the effects of extracts of the pituitary and of epinephrin; this is, however, only superficial. The effect of epinephrin upon organs containing smooth muscle is always the same as that of the stimulation of the sympathetic nerves supplying these organs; when the sympathetic causes inhibition instead of contraction, epinephrin does the same. The effects of pituitary extracts are entirely independent of the sympathetic nerves; they are exerted directly upon the muscle cells (Dale, 47). Hence, the effects of the two drugs are in many in-

stances different. Thus, the pituitary causes marked constriction of the coronary and pulmonary vessels; epinephrin has but little effect upon these. Pituitary always causes marked contraction of the uterus, whether this is pregnant or at rest; the effect of epinephrin depends upon the sympathetic innervation, and so, under some circumstances, causes a relaxation. Epinephrin stimulates the endings of the sympathetic nerves of the heart, causing an acceleration and augmentation of the heart beat; pituitary extract causes a slowing and at first a strengthening of the beat, but this soon gives place to a weakening. The latter effect is probably due in part to the constriction of the coronaries; this is antagonized in the intact animal by the rise of blood-pressure, so that the secondary weakening of the beat is not usually observed.

Howell made the interesting observation that a second injection within one-half to one hour does not cause a second rise of blood-pressure; it may cause a fall. Later a rise is again observed; this observation is of importance in connection with the therapeutic use of the extract.

v. Frankl-Hochwart and Fröhlich (215) found an increased irritability of the autonomic motor nerves of the bladder to faradic stimulation. Similarly, the irritability of the hypogastric nerves to the uterus was much increased. These effects were produced only by the first injection of the extract.

Magnus and Schäfer and Schäfer and Herring found that the intravenous, subcutaneous, or intraperitoneal injection of extracts of the posterior lobe caused marked and long-continued diuresis and dilatation of the kidneys. Administration by the mouth also increased the amount of urine secreted, both in animals and in man (193). Schäfer found that stimulation of the hypophysis by injury caused marked polyuria in dogs. He believed that the polyuria often occurring in acromegaly is due to an involvement of the posterior lobe.

There has been considerable discussion as to whether the diuresis is due to a direct action upon the cells of the kidney, or is brought about indirectly through changes in the circulation.

Ott and Scott (161) and Schäfer and Mackenzie (194) found extracts of the posterior lobe to markedly increase the secretion of milk.

Goetsch, Cushing, and Jacobson found that the injection of extracts of the posterior lobe caused a lowering of the tolerance for carbohydrates; this effect was especially marked in animals, in which the carbohydrate tolerance had been increased by the previous extirpation of the posterior lobe.

Repeated daily injections of extracts of the hypophysis are very deleterious, leading to rapid emaciation and to tissue changes, especially in the liver; these effects are chiefly due to the posterior lobe.

Mairet and Bosc, Parisot, and Delille found that malaise, slight elevation of temperature, slowing of the heart, rise of blood-pressure, and

diuresis followed the administration of the entire gland by mouth or injection. Harvey (87) found sclerotic changes in the coronaries after repeated injections of pituitary extracts.

The active principle or principles of the hypophysis have not been isolated, and little is known as to their chemistry. They are dialyzable, are not destroyed by boiling, and are not soluble in alcohol and ether; they resist peptic but not tryptic digestion. They do not give the color reactions characteristic of epinephrin, although they seem to give certain decomposition products analogous to those of this compound. The pressor principle is excreted, to some extent at least, unchanged in the urine.

The commercial preparation "pituitrin" is an extract of the posterior lobe: one c. c. corresponds to 0.1 gram of the fresh, or to 0.01 gram of the dried, gland.

Summary.—The above observations and experiments show that the anterior lobe of the hypophysis is a structure essential to life, the removal of which leads in a short time to death, the partial removal or disease of which leads to a condition of retarded growth or infantilism, to obesity, to atrophy of the sex glands, and other disturbances of nutrition. The hyperactivity of the anterior lobe (in acromegaly and gigantism) leads to accelerated and abnormal growth, and also to atrophy of the sex glands. It is believed to produce an internal secretion passing directly into the blood. Nothing is known as to the nature of the action of this part of the hypophysis; why the gland is so immediately necessary to life is especially obscure.

The posterior lobe and *pars intermedia* contain a substance or substances having marked effects upon plain muscle, especially that of the blood vessels, upon the kidney, and upon carbohydrate metabolism; while it thus has important pharmacodynamic actions, its rôle in the normal animal is obscure.

Especially marked are the relations between the hypophysis and certain other organs of internal secretion, the sex glands, the thyroid, and perhaps the suprarenals.

Therapeutic Uses of the Hypophysis

Organotherapeutics.—The earliest attempts to use the hypophysis in organotherapeutics were in connection with acromegaly. The results were very variable; many physicians obtained negative results, several reported distinctly favorable results, while a few reported injurious effects. A case described by Osborne (156) may be cited as an example of the favorable results sometimes obtained: Under treatment with hypophysis (six to twelve grains daily), the headache, which had been continuous for two years, was rarely present, appetite improved, muscular weakness and

nervous restlessness disappeared, and the patient was able to do her usual work, which she was not able to do before the use of the pituitary substance. The hypertrophy of the soft parts of the face, hands, and feet greatly diminished. On stopping the treatment the headaches and muscular weakness again developed, and the face and hands very noticeably increased in size. Similarly favorable results were reported by Kuh (116) in two of three cases, and by a number of other writers (49).

The recent work of Cushing and his coworkers suggests that it may be possible to determine when there is a change from hyperactivity to hypoactivity, at least as far as the posterior lobe is concerned: hyperactivity is accompanied by diminished carbohydrate tolerance or by glycosuria, whereas in hypoactivity there is an increased tolerance for carbohydrates. Hence, the administration of hypophysis in a case showing glycosuria or diminished carbohydrate tolerance would seem to be contraindicated. Goetsch, Cushing, and Jacobson suggest that it may be possible not only to define more accurately the cases of hypopituitarism in which hypophysis medication is indicated, but to obtain some conception of the desirable dose by a determination of carbohydrate tolerance. To illustrate the latter point they cite a case of hypopituitarism in which the tolerance for levulose was 150 grams; they estimated that the normal tolerance for a person of the patient's weight would be about 120 grams. The latter amount of sugar was given each day with gradually increasing doses of hypophysis. When the dose of the latter was increased to six grains (whole gland) three times a day, sugar appeared in the urine; they considered this to be the therapeutic dose in this case, as it was just sufficient to restore the normal limit for sugar.

In addition to acromegaly, hypophysis has been administered to a number of cases of *dystrophia adiposogenitalis* (Delille, 49). In some cases improvement, as indicated by diminution of the adiposity and stimulation of the sex glands, was noted; in many cases, however, the results were negative.

The administration of hypophysis has also been followed by improvement in cases of hypophyseal tumor, the symptoms of which could not be definitely classified, and in certain cases of obesity (Delille).

Cushing believes that there are many cases of hypoactivity of the pituitary, very often overlooked, in which the administration of hypophysis is indicated. He believes that an internal hydrocephalus, of whatever origin, is the most common source of moderate grades of this condition; a beginning adiposity and increased carbohydrate tolerance are very suggestive symptoms.

Therapeutic Uses of Extracts of the Posterior Lobe (*Pituitrin*).—Extracts of the posterior lobe are used chiefly for their effects upon plain muscle, especially that of the uterus and blood vessels. The nature of this action has already been discussed.

Many recent writers (1, 60, 76, 203) have reported very favorable results from the use of such extracts in *uterine atony,* and in *post-partum* and other forms of *uterine hemorrhage;* several claim that it has distinct advantages over ergot in these cases. Foges and Hofstätter and Hofbauer lay especial emphasis upon the increased irritability of the uterus (sensitizing action of Frankl-Hochwart and Fröhlich); slight stimuli cause a long-continued contraction. Bab (11) suggests that its effects on uterine hemorrhage may be due in part to its causing a diminution of the activity of the ovaries; the same idea has led him to employ it in cases of osteomalacia with, he states, much improvement in several cases.

Several writers have advocated the use of pituitary extracts to increase the blood pressure in shock and various infectious diseases (pneumonia, diphtheria, typhoid, etc.), claiming that it has the advantage over epinephrin of a much more lasting effect (Mummery and Symes, 148; Mummery; Williams 230; Klotz, 110). Wray (233) stated that in postoperative shock the improvement in the circulation may last twelve to fifteen hours after the intramuscular injection of one c. c. of the twenty per cent. solution of the posterior lobe.

Wiggers (229) considers that it is the only drug which meets the indications for a hemostatic in pulmonary hemorrhage, since it raises the blood pressure from peripheral action (which constricts the bleeding points and at the same time prevents anemia of the brain), and causes a weakening of the heart, which prevents a rise of pressure in the pulmonary vessels.

Bell (19) recommended it in intestinal paresis after abdominal operations; he states that it acts more powerfully on the paretic than on the normal intestine.

Klotz considers it especially valuable in peritonitis, where it not only increases the blood pressure, but stimulates peristalsis.

The vasoconstriction is not very marked when applied locally, but it has been recommended in hay fever.

Pal (162) reported excellent results from the use of the extract in a case of severe tetany in a boy.

The drug has been injected subcutaneously or intramuscularly in doses of one to three c. c. of the aqueous extract, one c. c. corresponding to 0.1 or 0.2 gram of the fresh gland (posterior lobe), or intravenously in doses of one to two c. c. diluted with twenty c. c. normal saline solution. There is stated to be some danger of local necrosis when injections of strong solutions are made subcutaneously. It has also been given by the mouth in doses corresponding to 0.2 gram to 0.8 gram of the fresh gland, or one to three grains of the dried gland (posterior lobe).

The drug is contraindicated in conditions of high blood pressure.

Although untoward results from its medicinal use do not seem to have been reported, it should be remembered that Harvey has produced

sclerotic changes in the coronary vessels of animals; Crowe has seen loss of weight and marked changes in the liver from repeated injections; Thaon (207) reports pathological changes in the kidney after prolonged use of large doses, and Franchini (63) has observed intestinal ulceration and hemorrhage.

PANCREAS

The use of the pancreas or of preparations of it as an organotherapeutic agent has met with little or no success, although there is conclusive evidence that this gland produces an internal secretion of vital importance, the disturbances of which play an important part in diabetes mellitus. It is unnecessary to review in this place the evidence for the existence of such an internal secretion and the reasons for believing it to be formed in the Islands of Langerhans, nor to discuss the various hypotheses as to how it acts.

Administration of Pancreas Preparations by the Mouth.—Some of the earliest attempts to treat diabetes mellitus organotherapeutically were by the administration of the pancreas by the mouth; it was early largely abandoned, for the results were practically negative. Mackenzie (134), Wood (232), White (225), and de Cerenville (48) are among those who have published reports on this subject; some of these also reported experiments on the injection of extracts subcutaneously.

A few writers (43, 41) have reported favorable results. Some of these reports contain only impressions; in others the glycosuria seemed dependent upon an infection, and varied so much in severity that it is difficult to determine what, if any, effect the treatment had. In Cowles' case the diabetes had followed an abscess of the pancreas; marked and rapid improvement is stated to have followed the eating of one to six (average three) raw pancreases of calves daily; after discontinuing the treatment the patient became rapidly worse and died.

Rennie and Fraser (182) administered the Islands of Langerhans obtained from fish of certain species in which they occur separately, i. e., distinct from the pancreas proper, to a number of diabetics; the results were inconclusive.

Sewall (199) found in the earlier stages of a case of youthful diabetes that the urine could be made free of sugar by the administration by mouth of infusions of raw, lean beef followed after some hours by one of pancreas; neither alone was efficacious, and after some months the combined treatment failed. The method was ineffective in a number of other cases. No good results attended the use of the commercial pancreatic powder.

Observations on the effect of administering pancreas in experimental pancreatic diabetes of animals also afford little ground for hope (Rosenberg, 187). In fact, the administration of the gland to dogs deprived

of their pancreas has frequently aggravated the glycosuria. Sandmeyer (192), for example, found the sugar increased three to four-fold in such experiments. Pflüger (169) obtained similar results.

Somewhat more encouraging results were obtained by Pratt and Spooner (177), who studied the effect of feeding fresh pancreas to a dog with lowered limit of assimilation for glucose; the lowered assimilation limit was secured by producing atrophy of the pancreas by ligating the ducts and separating the pancreas from the duodenum. There was, however, no glycosuria. The assimilation limit rose rapidly and steadily during the administration of two or three raw pancreases per day; it was increased by more than one hundred per cent. There was a gain of weight. Six weeks after the last pancreas had been given the assimilation limit was greater than that in any normal dog studied; the authors state that it would be futile to speculate on the cause of this increase until more experimental data have been accumulated. Pratt stated that the feeding of fresh pancreas or of pancreatic preparations does not diminish the glycosuria in ordinary diabetes, and Pratt and Spooner (178) reported a case of undoubted pancreatic diabetes in man in which the daily administration of a large amount of raw pancreas for a month had no effect on the glycosuria.

There is, however, according to Falta (57), a small group of cases of human diabetes in which the administration of pancreas by the mouth gives good results; this is the result of supplying the external and not the internal secretion of the gland. Falta refers to those cases in which the pancreas is diseased, so that there is no longer an adequate secretion of pancreatic juice into the intestine; this occurs most frequently when lithiasis causes complete obstruction of the pancreatic duct. In such cases Falta states that the administration of large doses (ten grams daily) of pancreatin gives excellent results; calcium carbonate is given at the same time.

Subcutaneous and Intravenous Injections of Pancreas Preparations; Transplantation.—A number of attempts have been made to treat diabetes by subcutaneous and intraperitoneal injections of extracts of pancreas. The favorable results reported in some of the earlier of these were shown by Pflüger (168) to be wholly inconclusive. The more recent attempt of Zuelzer (235) to treat the disease by the intravenous injection of a "pancreas hormone" was shown by von Fürth and Schwarz (216) to be based upon a very unsatisfactory theory, and by Forschbach (61) to be apparently accompanied by danger.

Similarly, all attempts to check diabetes in animals by the injection of extracts of the pancreas have resulted in failure.

The transfusion of blood from a normal into a diabetic animal has resulted in a diminution of the glycosuria of the latter only under the most exceptional circumstances; it is doubtful if it has ever succeeded

except in some experiments of Hédon. Hédon (88) has recently found that when the *processus uncinatus* of the pancreas of a normal dog was perfused by the splenic vessels of a diabetic dog, the urine of the latter became free of sugar; there was, however, but a slight diminution of the sugar in the blood. The fact that the latter did not increase indicates that there was a diminished formation or an increased destruction of sugar. No effect was obtained when the pancreas was perfused from the carotid of the diabetic dog; it seemed to be necessary for the blood, to be effective, to pass from the pancreas directly to the liver through the portal circulation. Hédon also found a diminution of sugar in the urine when blood from a normal dog was injected directly into a vein of the mesentery; there was no effect when it was injected into the general circulation. These seem to be the first cases in which the internal secretion of the pancreas has been shown to have any effect upon experimental diabetes; they were, however, obtained under conditions so far removed from anything which could be attained in human diabetes that they make the successful treatment of the latter by the internal secretion of the pancreas seem more problematical than ever.

As a consequence of these various negative results the suggestion has been offered that the internal secretion of the pancreas passes into the blood as rapidly as it is formed, in somewhat the same manner as the urea formed in the liver is secreted at once into the blood; so that there is no accumulation of the internal secretion in the gland available for therapeutic purposes. The rapidity with which glycosuria appears in animals after removal of the pancreas (1½ to 5 hours) (Bierry and Gatin-Gruzewska, 25) would seem to indicate that there is not very much of the internal secretion in the blood at any one time, and also that it is immediately necessary for normal carbohydrate metabolism. Another suggestion to account for the failure of organotherapy is that the internal secretion is not secreted in a finished form, but that it must be activated in some manner by some other organ, and that it has hitherto been impossible to accomplish this, and also that it is a very unstable body, easily destroyed by the manipulation of the gland.

Transplantation experiments in the lower animals also offer no prospect of successful treatment of diabetes by this means.

Transplantation.—The transplantation of the pancreas from one mammal into another, even of the same species, usually results fatally in a day or two (v. Bergmann, 213; Gulecke, 80), the fatal result being due to the liberation of trypsin.

Pflüger's (168) attempts to check pancreatic diabetes in frogs, by the transplantation of the pancreas of a normal frog, were entirely unsuccessful, as were also Hédon's experiments on dogs.

The "successful transplantation" experiments in animals have been preventive, and not curative, and in most cases part of the animal's own

(normal) pancreas was transplanted. The exact mechanism of this preventive action has been much discussed (Lombroso, 129). In those cases in which the transplantation was successful two operations were performed: part of the pancreas, with its mesentery, vessels, and nerves, was drawn out of the abdominal cavity and sutured under the skin; after this graft had grown the remainder of the gland was removed; no glycosuria resulted until the graft was extirpated. Hédon (89) found that in nearly all cases simply cutting the nerves and vessels without removing the graft was sufficient to cause glycosuria. Martina separated a portion of the pancreas of a dog entirely from its nerves and vessels, and transplanted it into the spleen; the dog survived the extirpation of the remainder of the gland for an unusually long period (four months), but diabetes was not prevented.

Minkowski (144) has reported new experiments on the transplantation of the pancreas. If a graft secures a sufficient blood supply it grows and functions to such an extent that the animal's own pancreas may be completely removed without the occurrence of diabetes. The transplantation must be made before diabetes has been induced, otherwise healing of the wound will not take place.

Fortunately few attempts have been made to treat human diabetes by transplantation of the pancreas. Futcher (71) states that Williams, of Bristol, transplanted the pancreatic gland of a sheep under the skin of the breast and abdomen of a diabetic. The patient died in three days of coma.

SEX GLANDS

The first experimental demonstration of the existence of internal secretions was made in connection with the sex glands (Berthold's experiments on capons in 1849), and the first definite and conscious attempt to utilize them for therapeutic purposes was also made in connection with these glands (Brown-Séquard's experiments with testicular extracts, 1889).

Experimental and clinical work has demonstrated conclusively the presence and importance of internal secretions in both the ovaries and testicles. It has also been shown that they originate in parts of the glands other than those producing the external secretions; in the male they probably originate in the interstitial cells of Leydig (Hanes, 85), whereas opinions differ as to their origin in the female, but it is generally accepted that the corpora lutea constitute one important source.

The functions of the internal secretions of the sex glands are chiefly connected with sexual life; they control the development and maintain the integrity of the accessory organs of generation and of the secondary sex characters; internal secretions of the ovaries cause the changes in the

uterus which follow the impregnation of the ovum; menstruation is also dependent upon them.

In addition to such specific actions the internal secretions of the sex glands have other, undifferentiated, effects, such as an influence upon growth (especially of bone) and upon metabolism (increased oxidation, especially in castrated animals). They also have reciprocal relations with many other organs of internal secretion (hypophysis, thyroid, thymus).

Therapeutic Uses of the Sex Glands

At present the sex glands are used as organotherapeutic agents almost exclusively in gynecology, and their discussion properly belongs in special works on this subject. It seems probable, however, that with increasing knowledge of the relations of these glands to various functions and to other organs of internal secretion they may also acquire a considerable importance in connection with internal medicine. Thus, the relations of the ovaries to the hypophysis promise to be of practical as well as of theoretical interest. Fichera stated that the hypertrophy of the hypophysis which occurs in animals after removal of the ovaries may be checked by the administration of ovary. Such results suggest that ovary might be of value in cases of dyspituitarism, and Moffitt (145) has reported a case with obscure symptoms suggestive of dyspituitarism which improved markedly under ovarian therapy: the indefinite nervous symptoms disappeared and menstruation became more nearly normal.

The ovary, or preparations of it, is chiefly used to combat the disturbances occurring at the menopause, natural or artificial. Many writers report very favorable results in such cases (7, 51). The attacks of giddiness, trembling, palpitation, flushes, sweatings, and other nervous and vasomotor disturbances, which may occur many times in a day, were reported to be much reduced in number and severity, or to have ceased entirely in some cases. The best results are obtained in cases of post-operative menopause, especially in young women. Relapses frequently occur after stopping the treatment.

Many cases have been reported in which the results were negative, and in some of those with improvement suggestion may have been an important element. Various disturbances of the skin (acne, eczema, and prurigo) occurring during the menopause are often benefited by it (191). It has also been found of value in certain cases of acne in girls. Its use in amenorrhea and dysmenorrhea has not been very encouraging; more favorable results have been reported in amenorrhea with chlorosis. The latter is believed to be associated with disturbances of ovarian function.

Ovary has also been recommended for various vague symptoms (insomnia, headache, depression, pains in the back) associated with ovarian and uterine diseases.

In recent years corpus luteum has been used somewhat extensively instead of the entire gland; it was introduced by Fränkel on the theory that it exerts throughout sexual life a trophic action on the uterus. Recent investigations (Loeb, 125) show that the corpus luteum produces an internal secretion which leads to a hypertrophy and softening of the uterine mucosa, and sensitizes it so that it reacts to a foreign body (or ovum) with the formation of a maternal placenta; all attempts to obtain this effect from injection of extracts have failed (Loeb; Frank, 65). It has also been shown that the corpus luteum inhibits or delays ovulation, but this action is exerted entirely in the ovary itself. Thus, there seems to be little experimental basis for the therapeutic use of corpus luteum in cases in which the ovaries have been removed, but the entire subject is so obscure that it is much better to base practice upon clinical experience than upon theory. Clinical experience, however, has not been uniform (McDonald). Fraenkel (62) reports more or less favorable results in ninety-one per cent. of ninety-six cases of disturbances of the menopause, etc.; the drug had no effect in dysmenorrhea, irregular menstruation, and the intoxications of pregnancy.

Maits (138) reported favorable results in "osteomalacia, disturbances of the natural and artificial menopause, and in hypofunction due to infantile uterus."

Recently it has been especially recommended in cases of amenorrhea and scanty menstruation, and when there are nervous symptoms which may be due to this insufficiency. It is said to markedly increase the menstrual flow and to prevent nervous conditions accompanying their functional deficiency.

Testicles.—The first attempts to consciously utilize the internal secretion of the testicle were made by Brown-Séquard in 1889, who reported remarkable results from the subcutaneous injection of testicular extracts. They were said to increase bodily and mental vigor, to have a favorable regulating influence upon the intestines, etc. Many other reports have been published along these lines, but they have little scientific value; many of the results claimed were evidently due to suggestion.

Zoth (234) and Pregle (179) endeavored to demonstrate, objectively, an effect of testicular extracts upon muscular activity. They stated that the subcutaneous injection of such extracts, combined with muscular exercise, led to a marked increase in the amount of work which could be accomplished, and also to a diminution of the sensation of fatigue.

Recent scientific literature contains few references to testicular extracts.

Preparations and Dosage

Practically nothing is known as to the chemistry of the internal secretions of the sex glands. Loewy (127) tested the efficiency of various

extracts of the ovaries upon a castrated bitch which reacted to the administration of ovarian substance by an increase in metabolism: glycerin extracts were especially active, saline extracts less so, whereas acids and alcohol seemed to destroy the activity.

The gland (usually of the cow or hog) has been administered in the fresh and dried state, and in the form of various extracts, both orally and subcutaneously. At present it is used most frequently in the form of the dried powder, in doses of 0.06 to 0.5 gram (one to eight grains) or more, three or more times a day. Many writers seem to have employed too small doses. As it sometimes causes disturbances of digestion, its use should be interrupted at times. Einhausen recommended gradually increasing the dose to five grams (75 grains), or more, per day, and continuing this for some time after an effect is obtained, and then gradually decreasing it for a time.

The dried gland is frequently administered in the form of tablets; the designation of the weights of the commercial tablets is as lacking in uniformity as in the case of thyroid tablets.

The dried powdered corpus luteum (also called "lutein") has been administered in doses of one-half to two grains (0.03 to 0.12) or more three times a day. It has been used in the form of various extracts (50). Maits used a sterile one per cent. extract of the corpus luteum in normal saline solution injected subcutaneously in doses of ten c. c.

The contradictory results reported in regard to ovary therapy may be due in part to variations in the character of the gland used; as Marshall (140) suggests, "it would seem unreasonable to expect to obtain uniform results from the indiscriminate usage of ovaries in different stages of cyclical activity (e. g., ovaries with prominent follicles like those from animals 'on heat,' or ovaries with corpora lutea like those of pregnant animals, or ovaries in a state of relative quiescence like those of anestrous animals)."

The ovaries of many of the lower animals also differ markedly from those of man, in accordance with the differences in the sexual lives.

MAMMARY GLAND

There is not much evidence that the mammary gland has an internal secretion beyond the fact that menstruation is usually in abeyance at the height of mammary activity. There is, however, some evidence that it contains substances (perhaps internal secretions) which have distinct effects upon metabolism and upon other organs. Thus, Hunt showed that, when it is administered by mouth to animals, it causes changes in metabolism analogous in certain respects to those caused by thyroid.

There is some clinical evidence that the administration of mammary

gland has an effect upon the uterus. Thus, it is stated (155) to give excellent results in the profuse menstruation of young girls when there is no apparent uterine reason, and also in too frequent menstruation; it is said to be partially efficient in shortening a prolonged flow.

It is recommended in doses of five to ten grains three times a day.

THYMUS

Functions of the Thymus.—The thymus has important relations to the sex glands and to growth, especially to that of bone. It also seems to have some special relation to the thyroid. At least some of these relations are believed to be maintained by means of internal secretions.

The thymus exerts its action only during early life. It is relatively largest shortly after birth, when it constitutes about four per cent. of the body weight. It continues to increase slowly in absolute weight until puberty, after which it decreases, and is finally largely replaced by fat. The relation of the thymus to the sex glands suggested by its changes in weight is further illustrated by the effects of castration upon the thymus and the effects of removal of the thymus upon the sex glands. Henderson (91) found that early castration caused a further growth of the thymus and a prolonged or delayed involution; involution occurred especially rapidly in animals used for breeding purposes. On the other hand, Paton (164) stated that removal of the thymus in sexually immature animals led to a rapid growth of the testicles. From the above experiments and observations it has been concluded that the thymus exerts an inhibitory action upon the development of the sex glands, and, on the other hand, that the development of the sex glands has an accelerating effect upon the involution of the thymus. Paton (165) concludes from more recent experiments that thymus and testes both exercise an influence on the growth of the sexually immature animal; the removal of both retards growth. After removal of one the other can compensate for its loss, and in doing so may undergo a more rapid growth, or, in the case of the thymus, may persist for a longer period. Further evidence of a relation between the thymus and sex glands has been sought in the statement that the ovaries are frequently enlarged in *status lymphaticus* (Bartel and Herrmann, 13).

The relation of the thymus to growth was studied by Basch (14, 15) and others (86, 130) in young animals from which the thymus was removed. Such animals showed delayed growth and diminished intelligence. The changes in the bones were especially marked; these showed deficient ossification. Basch also reported that the peripheral nervous system showed an increased excitability, as determined by galvanic stimulation.

Klose, and Klose and Vogt (109) found that, if the thymus were removed from puppies about ten days after birth, there was a latent period

of two to four weeks, then a condition of adiposity for two or three months, followed by cachexia and a condition resembling idiocy, and death in "thymic coma" after three to fourteen months; they say that extirpation of the thymus in infants is followed by similar results. They consider the gland to be a vital organ in early life. They also found that the bones of animals deprived of the thymus had but about half the normal amount of calcium. They consider the bone and other changes to be due to acid intoxication, and that one of the functions of the thymus is to inhibit the formation of or to neutralize an excessive formation of acid, probably nucleic acid. The administration of thymus to dogs deprived of these glands was said to greatly hasten the effects of thymectomy.

The thymus is very often found persistent or enlarged in cases of Graves' disease, especially in the severer forms. Capelle and Bayer (36) believe that an internal secretion of the thymus aggravates the symptoms, especially the cardiac symptoms of this disease. They report improvement from thymectomy. Bircher (27) stated that the implantation into animals of a pathological thymus caused symptoms of Graves' disease, such as tachycardia and tremors.

Rachford (180) believes that the thymus produces an internal secretion affecting nutritional processes, especially in fetal life and early childhood; he believes that *status lymphaticus* is due to an excessive activity of the thymus, as Graves' disease is believed to be due to an excessive activity of the thyroid. Friedlander (68) stated that exposure of the thymus to Röntgen rays caused diminution of the size of the spleen and lymph nodes in *status lymphaticus*.

Therapeutic Uses of the Thymus

In view of the very unsatisfactory condition of the knowledge of the function of the thymus, it is evident that a rational organotherapeutics is impossible; clinical trials have not led to conclusive results. Thymus has been administered in many conditions (gout, various forms of thyroid disease, acromegaly, Addison's disease, etc.). Especial emphasis has been laid upon its value in rickets and, recently, in metabolic osteoarthritis; Nathan (150) administered it in doses of two to four "5-grain" tablets (each tablet apparently containing dry gland equivalent to five grains of the fresh gland) three times a day for long periods.

Favorable results (delayed growth and relief of pain) have been reported from its use in carcinoma (81). It has been administered by hypodermic injection of extracts and by the mouth. Gwyer administered it by the mouth in doses of from 30 to 120 grains (2.0 to 8.0) of the dried powder three or four times a day; Takaki used far smaller doses and stated that gastric disturbances frequently occurred during its use.

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CHAPTER III

VACCINE AND SERUM THERAPY

FRANCIS CARTER WOOD

A. HISTORICAL

The fact that individuals who recover from certain infectious diseases are immune has been known since the earliest times, and was noted by Thucydides in relation to the plague at Athens. In China, practical application of the observation was made as early as 1000 A. D. by exposing children to smallpox or actually inoculating them with dried lymph, in order to produce a mild form of the disease, which they usually survived, and which rendered them immune. Among certain castes in India and some of the wild tribes of Africa it was the practice to immunize individuals with small doses of snake venom as a protection against subsequent bites. Smallpox inoculation was introduced from Asia among Western nations in the eighteenth century. Inoculations of cowpox as a protection against smallpox had also been practiced in England and on the Continent in isolated instances; but it was not until Jenner had made his observations that the value of the method was established, and the procedure generally introduced.

Further advances in immune therapy were not made until Pasteur's work, nearly a century later. From his studies on experimental infections, based on Jenner's observation that immunity to smallpox could be produced by attenuated virus, Pasteur concluded that this might be a general law applicable to other infections. Acting on this theory he was able to immunize fowls against chicken cholera. He also developed methods of vaccinating against anthrax and swine erysipelas, each instance requiring some special method of attenuating the virus. He found that he was able to diminish the pathogenicity of parasites for their natural host, not only by cultivation and preservation under unfavorable conditions, but also by repeated passage through other animals; and that, while passage through some species might diminish the virulence, passage through other species might enhance it, and modify the type of disease produced and the length of the incubation period. Owing to the rapidity of reproduction in the

low forms of life, to which these parasites belong, the results of natural or artificial selection so induced rapidly become more or less permanent, and are thus transmitted to successive generations of the organism, often for a long period.

The shortening of the incubation period in rabies, which occurs after passage of the virus through rabbits, gave Pasteur a means of combatting street rabies, which has a long incubation period, by immunizing the subject after infection. In 1885, after many experiments on animals, he made his first inoculations in man with success.

In 1892 Haffkine developed a similar method of vaccinating against cholera with the living vibrios attenuated by long culture. This procedure was made possible by the fact that cholera bacilli do not produce the disease when introduced subcutaneously, but only when given by mouth.

All the methods introduced by Pasteur depend on active immunization with attenuated living virus. By this means he was able to control three of the epizoötic diseases prevalent in France, and to reduce the mortality of rabies in man to a minimum; but, unfortunately, it has not been possible to extend the application of this principle materially, and all important advances have since been made with other means of active immunization.

It was shown by Salmon and Smith (128), in 1886, and independently by Chamberland and Roux, in the following year, that it was not necessary to introduce living microorganisms in order to produce immunity, and that the same result could be obtained by injecting bacteria killed by heat, or even by injecting culture fluids from which the bacterial cells had been removed by filtration.

In 1890 Koch introduced his original tuberculin as a specific cure. He believed that he had separated from the bacilli a directly curative principle which "killed the tuberculous tissue, but not tubercle bacilli." The effect he produced would now be ascribed to a local anaphylactic reaction. In 1897 he prepared a new tuberculin from finely pulverized bacterial cells, with a view to producing an active immunity against the bacteria by means of this extract.

Vaccination by the use of cultures killed by heat or antiseptics was introduced by Kolle in 1896 as an improvement on Haffkine's cholera prophylaxis. In the same year Wright introduced the use of killed cultures for immunization against typhoid fever, and two years later Shiga applied the procedure to dysentery with moderate success.

All of these procedures, except Koch's, were prophylactic, but in 1904 Wright introduced active immunization as a therapeutic measure in many chronic infections. He used, for the most part, cultures of the specific organism killed by heat, and when possible prepared his vaccine from strains isolated from the lesion to be treated. He also used Koch's new

tuberculin in minute doses, considering it not as a direct means of cure, but as an antigen against which immunity could be produced.

Far more marked success from a therapeutic point of view has been obtained by passive immunization. The production of antitoxic sera was made possible by the discovery, by Roux and Yersin in 1889, that the injury caused by infection with the diphtheria bacillus was chiefly due to a soluble toxin which the bacillus produced in culture as well as in the animal body. The same was shown by Knud Faber (1890) to be true of the tetanus bacillus.

We owe to von Behring the discovery that antitoxic immunity can be transferred from one animal to another by injection of blood serum. In 1890 he succeeded in immunizing animals against the tetanus and diphtheria toxins, and in protecting other animals from the fatal results of infection, by injecting them with the serum of immune animals. In 1893 von Behring first introduced his antitoxin for use in human diphtheria. The wonderful results which he obtained have led to innumerable attempts to apply the same principle to the treatment of other conditions; but these attempts have, for the most part, been unsuccessful; although Calmette, in 1894, developed an antitoxin for snake venom which is fairly effective, and tetanus antitoxin is valuable in prophylaxis.

The discovery of bacteriolytic immunity gave rise to the hope that bactericidal sera would prove as effective as diphtheria antitoxin. Attempts to apply such sera to the treatment of a great variety of infections met with slight success until 1906, when Jochmann introduced the treatment of epidemic meningitis by intraspinal injections of a serum which combined antitoxic with antibacterial action, a procedure since perfected by Flexner.

B. THEORIES UPON WHICH IMMUNE THERAPY IS FOUNDED

The methods of vaccination introduced by Jenner and Pasteur were based on the observation that survival after a modified form of a disease resulted in protection, but they did not analyze thoroughly the nature of this protection. The further application of immune methods has been the result of innumerable investigations into the mechanism of immunity, some of which may be briefly mentioned. In 1883 Metchnikoff advanced the theory that resistance to disease was due to the activity of phagocytic cells, which ingested and destroyed the invading parasites; and that immunity consisted in an increased activity of these phagocytes. Von Behring's discovery in 1890 that antitoxin is a soluble substance present in blood serum showed the inadequacy of this explanation; and it was soon found that immune serum possessed other specific properties. In 1893 Pfeiffer (114) demonstrated its bacteriolytic power when injected into the peritoneum of normal guinea-pigs, and in 1895

Metchnikoff (106) demonstrated the same property in vitro, though he believed that the immune substances were set free in the serum by disintegration of leukocytes. In the same year Denys and Leclef showed that even the increased activity of the leukocytes of an immune animal was due to substances in the blood serum, and not to any changes in the leukocytes themselves. Bordet (21) added to our knowledge of bacteriolysis by showing that two distinct substances, *substance sensibilisatrice* (amboceptor) and *alexin* (complement), take part in the solution of bacteria, either being inactive of itself.

The most important attempt to explain the development and action of immune substances in serum was the so-called "side-chain theory" developed by Ehrlich (43) in 1897. He believed that these phenomena were essentially chemical reactions, and applied to immunity certain ideas which he had developed to account for the combination of food stuffs with body cells. According to his theory, toxin attaches to certain atomic groups or side chains, to use the terminology of organic chemistry, of the protein of the cells. These hypothetical side chains of the cell substance are called receptors, and the corresponding atomic groups in the toxin molecules are called haptophores. The relationship of the haptophores to the receptors is comparable to that of a key and its corresponding lock. The haptophore group of each toxin unites with a specific receptor in the cell molecule, which is incapable of attaching any other toxin. The toxin molecule possesses another atomic group, the toxophore, on which its poisonous action depends. This is, however, inactive until attached to the proper cell by means of the haptophore group. Antitoxin consists of receptor groups set free in the blood serum, and these free groups unite with the toxin and saturate its affinity for the body cells, thus preventing it from uniting with the cells and producing a toxic action. According to Ehrlich's theory, this union takes place according to the law of multiple proportions, and, if a given amount of antitoxin saturates half the toxin in a solution, twice this amount will saturate all of the toxin. This simple relation, however, cannot usually be demonstrated, though Ehrlich was able to explain the irregularities by assuming the existence of other bodies, toxoids, in the immune serum, which possess a haptophore but no toxophore group.

While Ehrlich's theory now seems inadequate in many respects, it has had an extremely important and profound influence on experimental work in immunity. Other theories have since been brought forward to explain the relations of toxin and antitoxin. Arrhenius and Madsen consider that these substances are partly dissociable compounds resembling a weak acid and a weak base, and that the reaction between the two is reversible, their union depending upon an excess of free toxin and antitoxin in the solution. The quantitative relations between the two are thus covered by the law of mass action. Bordet (20) and Biltz (17)

consider the combination, not as a true chemical union, but as being of the nature of an adsorption phenomenon. More recently, Abderhalden (1) and others have, by the use of polariscopic methods, demonstrated a true disintegration of some toxic substances by immune sera. It is hardly profitable here to go further into these theories, especially as we are still very far from a complete understanding of the nature of immunity; but a statement of some of the more generally accepted facts and theories will be of assistance in comprehending the therapeutic methods. For the sake of brevity, these will be stated somewhat categorically; but, as almost every point is the subject of controversy, one should remember that the following statements are not universally accepted as true.

C. NATURE OF IMMUNITY

I. Natural and Acquired Immunity

Most of the known diseases attack only certain species of animals; other species, even if artificially inoculated, are insusceptible or naturally immune. Among susceptible species certain families and certain individuals also enjoy immunity. The age of the individual sometimes bestows a degree of immunity which is more often relative than absolute. Such insusceptibility, which is congenital or the result of normal growth, is called *natural immunity*.

Even in susceptible individuals, infectious diseases frequently terminate in recovery, and persons who have recovered are to a greater or less extent resistant to future attacks of the same disease. This condition is called *acquired immunity*. We know that many, if not all, of these diseases are due to the invasion of pathogenic parasites, and conclude, therefore, that some change takes place in the body of the recovered patient which prevents the parasite from growing, or at least from producing its injurious effects. A similar change can often be induced by other methods, such as the injection of dead parasites or their metabolic products. If the subject be stimulated in such a manner to develop its own immunity, the resulting condition is called *active immunity*.

We can also, in many instances, transfer the protective substance by injecting the blood serum of an immune animal into a normal animal, producing what is called a *passive immunity*.

If the resistance depends on the ability to destroy the invading parasite, it is called *antibacterial immunity;* whereas, if it depends on the ability to neutralize the toxin of the parasite, which is not prevented from growing, the immunity is said to be *antitoxic*.

The reactions of an organism which render it immune are quite general in their nature, and are closely related to those by which food stuffs

are converted to its use. Protein substances are normally broken down into simple radicals in the alimentary tract before absorption, but, if they are introduced parenterally, that is, directly into the system without passing through the intestinal mucosa, while a considerable amount is excreted by the kidneys, the remainder undergoes a similar catabolic process in the body fluids or possibly in certain cells. The substances in the blood plasma or the tissue cells which attack the proteins differ from the ordinary digestive enzymes in being highly specific; or, in other words, the substance which breaks up one form of protein will not attack another. If exhausted by the introduction of a large amount of a certain protein they are in time reproduced in excess, so that the organism is able to dispose more promptly of a second dose of the same substance, but not of any other protein. This increased power to destroy or render innocuous any particular foreign substance is known as immunity. The chain of events is apparently the same whether the foreign substance is injurious or not. Moreover, unicellular parasites, such as bacteria, which gain access to the system, and emulsions of cells from another species if injected, induce the formation of bactericidal, cytolytic, and other immune substances by what is probably a similar mechanism.

Immunity then probably consists of an excessive development of certain normal properties. As a matter of fact, its extent is almost always relative, and even highly immunized organisms can usually become infected under especially unfavorable conditions.

II. Antibodies

Two explanations have been advanced to account for acquired immunity. The humoral theory attributes it to soluble substances in the blood serum, while, according to the cellular theory, it depends on the activity of phagocytic cells. Neither of these hypotheses satisfactorily explains the natural forms of immunity, and it is probable that other elements enter into many of the acquired types. Whatever may be the essential protective feature, we can demonstrate that, when an animal becomes immune, its blood serum acquires new properties which we attribute to the presence of specific soluble substances, called *immune bodies* or *antibodies*.

Any substance which, when introduced into an organism, can stimulate the production of such antibodies, is called an *antigen*. It may be an infectious or harmless bacterium, an animal cell, or a toxic or an innocuous protein. Toxins and enzymes of unknown chemical composition, certain glucosides and possibly certain lipoids may also act as antigens.

We infer the existence of antibodies entirely from the results they produce. They have never been isolated and we do not know their chem-

ical nature; but they are inseparable from one or the other of the serum proteins, and may have the same chemical characteristics. They are unstable compounds, being easily destroyed by heat and by various chemical agents. They are demonstrated and their approximate concentration determined by their reactions with the corresponding antigen, either in vitro or when transferred to the body of another animal.

The effect of antibodies on bacteria or cells is more easily observed than are their reactions with soluble substances. Among the immune bodies produced in response to the injection of these formed antigens, we identify the agglutinins, the lysins, and the opsonins or tropins. The *agglutinins* cause the cells to clump in masses, a result which does not seem especially protective. This effect is produced apparently by a simple substance, which is destroyed by heating to 70° to 75° C. The *lysins* disintegrate the cells and bring the constituents into solution. They have about the same resistance to heat as the agglutinins, but, in order to effect solution of the cells, they require the presence of *complement,* a substance which is much more sensitive to heat, which is present in normal serum, and which is not increased in immunization. Immune bodies of this type, which are inefficient without complement and are thought to act by uniting the complement to antigen, are referred to as *amboceptors.* We can sometimes determine that immune sera kill bacteria or cells, though we are not certain that they actually dissolve them. Such sera are called *bactericidal* or *cytotoxic.* Their activity also depends on the presence of complement, and the immune bodies are probably identical with the lysins. Moreover, we recognize that serum produces an invisible change in antigenic cells which enables leukocytes to ingest them, and that this property is increased in immunization. We attribute it to the presence of substances known as *opsonins* or *tropins.* The term opsonins is usually applied to substances in normal serum which are destroyed by heating to 56° C.; and the similar bodies in immune serum, which are more resistant to heat, are called tropins or immune opsonins. In some instances they do not induce phagocytosis except in the presence of complement. There is much doubt as to their nature, some observers claiming that they are identical with the lytic complement and amboceptor, and others, probably more correctly, that they are distinct substances.

If a soluble antigen is combined with the corresponding immune serum, the formation of a flocculent precipitate can frequently be observed. The antibodies responsible for this phenomenon are called *precipitins* or *coagulins.* These bear the same relations to heat as the agglutinins. The precipitin reaction is the only directly visible result of the combination of antibodies with soluble antigens, but there is evidence that other changes take place. It is probable that such antigens are often chemically disintegrated by immune sera; and it can be demonstrated that, in the combination of these two, complement is used up even when

no visible precipitate is produced. From this we infer the presence of a group of antibodies having the characteristics of amboceptor and resembling bacteriolysins. These are sometimes termed *albuminolysins* and also *complement-binding substances*. Another evidence of the action of immune serum is that a soluble toxin combined with the corresponding serum is rendered harmless apparently without disintegration of the toxin. In some instances it can be recovered, after breaking up the combination, with its poisonous properties unimpaired. The neutralizing substance merely prevents the toxin from uniting with the body cells and is called *antitoxin*. It is destroyed at a temperature of about 60° C.

III. Anaphylaxis—Hypersusceptibility—Serum Disease

The various immune bodies are not necessarily protective in their action, and certain bacteria, such as the cholera vibrio, may be more directly toxic after bacteriolysis than before. A more remarkable phenomenon was noticed by von Behring in his early work on diphtheria antitoxin; he found that horses immunized against diphtheria toxin sometimes became more susceptible to the toxin than normal horses, even when their serum contained sufficient antitoxin to protect other animals passively. This paradoxical condition has been called anaphylaxis, by which we signify a condition induced in an organism by treatment with an antigen, which, after a certain incubation period, renders the organism extremely sensitive to a second injection of the same substance. The reaction in a sensitized individual may be injurious and even immediately fatal, but is not necessarily so, and may result merely in the abrupt appearance of transitory symptoms, such as dyspnea or urticaria, after which the subject returns to a normal condition. Whatever the effect on the injected individual may be, the reaction usually results in a destruction of the invading parasite or antigenic substance, and may in this respect be beneficial. As the word anaphylaxis implies that the result is harmful, von Pirquet (115) has introduced the term "allergic" to denote any condition of altered susceptibility which causes an individual to react immediately or in a different manner to the second injection of an antigen.

The paradigm of anaphylaxis is the so-called Theobald Smith phenomenon: If a guinea-pig be injected with a foreign protein, as horse serum, in minute quantities, 0.01 to 0.001 c. c., and after seven to twelve days be given subcutaneously a second dose of 3 to 5 c. c., it develops severe dyspnea and paralysis, and dies in convulsions, usually within an hour. The dyspnea is probably due to spasm of the bronchi. If the second injection be made intraperitoneally, intravenously, or subdurally, much smaller doses are required to produce a fatal result, about 0.04 c. c. intravenously usually being sufficient. This hypersensitive condition has

been shown to persist for years, and is probably permanent. If a sublethal dose be given, the animal becomes dyspneic and usually has convulsions, but recovers its normal condition within a few hours.

Anaphylaxis may be produced passively by the injection of the blood serum of a sensitized animal into a normal guinea-pig. After a brief period of incubation, twelve to twenty-four hours, this second animal will react to the proper antigen in the same way as an animal sensitized in the original manner. Shock may also be produced in a normal guinea-pig by injecting a mixture of anaphylactic serum and antigen which has been incubated in the presence of complement.

The shock apparently occurs because the body is overwhelmed with toxic products formed by disintegration of the foreign protein, which ordinarily are produced in harmless quantities, but in an anaphylactic animal are produced suddenly in large amounts by an antibody present in the blood. A picture closely resembling anaphylactic shock can be produced by the intravenous injection of peptone into normal guinea-pigs.

A reinjected animal which has recovered from anaphylactic shock is temporarily insusceptible to future injections of the same serum, and for some time can not be resensitized. This condition of antianaphylaxis can also be induced by large injections during the latter part of the incubation period. It can not be passively transmitted; indeed, the serum of an anti-anaphylactic guinea-pig may produce passive anaphylaxis when injected into another pig. Antianaphylaxis may be produced in a sensitized animal by the injection of minute amounts of serum, intravenously, subcutaneously, or by rectum, and large injections can then be made without producing shock. It has been found possible to prevent shock by anesthetizing the animal before injection with ether, alcohol, or chloral, and sometimes by a preliminary injection of atropin.

Anaphylaxis is relatively specific. A guinea-pig sensitized by injections of sheep serum will react on reinjection to minute amounts of sheep or goat serum, to somewhat larger amounts of human or ox serum, and not at all to chicken serum. These animals may be readily sensitized to other animal sera, to white of egg, and to milk. They also develop a less characteristic anaphylaxis to toxins and to formed albuminous bodies, such as bacteria; and hypersusceptibility may be produced in other animals, though not so readily as in guinea-pigs. Inferences as to the action of protein in man can be drawn from these experimental data only with the greatest reserve.

Serum Disease.—A group of symptoms has been described by von Pirquet and Schick (116) in certain individuals following the injection of large amounts of horse serum. After a period of incubation of from eight to thirteen days, the patients develop an urticarial or erythematous rash, usually accompanied by slight fever and swelling of the lymph nodes in the region injected, and sometimes by painful swelling of the

joints, edema, and symptoms of renal irritation. The urticaria may involve the mucous membranes and cause slight dysphagia or dyspnea. The rash usually disappears suddenly, within three days at most, but has been known to last a week. After disappearance, it may recur with equal abruptness. This condition is called serum disease (Weaver, 151).

If such a susceptible individual is again injected within four months, there may follow an immediate reaction of a similar type without any incubation period; and usually the symptoms are more severe and may be accompanied by severe dyspnea, evidences of great vasomotor depression, and even syncope. Often there is an area of edema and congestion about the site of the second inoculation. In some instances the second injection results, not in an immediate response, but in an "accelerated reaction," that is, one occurring after an interval of less than eight days.

The severe and rapid reactions which occur after second injection after a proper interval are due to a condition of anaphylaxis, and are comparable to the shock produced in guinea-pigs. They are, however, much less frequent and severe than the reaction in these sensitive animals. As has been stated, the subcutaneous injection of 3 c. c. of serum into a sensitized guinea-pig is usually fatal, but the corresponding dose, 200 to 300 c. c., administered to man after an interval of one or two weeks, often produces no symptoms.

The relationship of serum disease following a first injection is less certain, but it is thought that enough of the foreign serum may remain in the system for eight days to react with the anaphylactic antibodies which are produced during this incubation period.

Sudden Death after Antitoxin Injection.—Since the introduction of diphtheria antitoxin, there have, however, been reported a few cases of sudden death following its use, about thirty-five in all; and, although extremely rare, these cases demand consideration. Most of the reports are fragmentary, but apparently death followed a first injection of serum in all instances, with the exception of two cases, in one of which it was attributed to a fourth injection made four days after the preceding one (Gottstein, 60); in the other to a second injection after an interval of a year (Dreyfuss, 39a). The majority of these accidents can not be explained as instances of anaphylaxis unless it is assumed that the individuals were sensitized in some other way, as by heredity or through the alimentary tract. This latter suggestion is highly improbable, as no deaths have been reported from certain districts where horse meat is used for food. Probably some of these deaths were not due to the serum at all, as the patients were moribund when injected, and, in other instances, exitus was caused by sudden strain on a heart much degenerated by the diphtheria toxin. There remain, however, certain cases in which death has followed prophylactic injections in apparently normal individuals. In some of these, autopsy disclosed a pronounced status lymphaticus, but others were unex-

plained. The possible connection of asthma with these accidents is of interest. Gillette (58) collected fifteen cases of sudden death, and thirteen of severe shock following injections of antidiphtheritic or antistreptococcus serum, in most of which there was a history of asthma or urticaria. In some patients these attacks had been regularly brought on by contact with horses. On the other hand, the writer knows of one individual with typical "horse asthma" in whom injections of horse serum did not produce the slightest symptoms.

While we recognize that these unexplained cases of death and shock do occur, we should remember their great rarity; in twelve years only two fatal cases were reported to the New York Department of Health, and many persons who have had extensive experience with antitoxin have not seen any alarming reactions. The risk of serum injection is much less than that attending the administration of many drugs, and should never weigh in the treatment of diphtheria or even in prophylactic injections when exposure to the disease is at all likely. It may, however, have some bearing on the indiscriminate immunization of normal individuals. In patients with a history of asthma or with suspected status lymphaticus it may be advisable to give a very small test dose, as described below in making reinjections, and to precede the therapeutic dose with the administration of 0.01 grain of atropin. So far as is known, true serum anaphylaxis is never fatal to man, but, judging from experience with laboratory animals, there may be some danger in giving a very large dose of serum to a patient after an interval of a week or more. There is certainly a slight possibility of producing severe shock. This is also true of rather moderate doses, if injected directly into the circulation. Besredka (15) has urged the use of very small preliminary injections in such cases to vaccinate the patient against anaphylactic shock. As has been stated, if an anaphylactic guinea-pig is given a minute amount of serum, it quickly develops a condition of antianaphylaxis, a fact first demonstrated by Lewis (93). Twice the dose ordinarily fatal will then produce no symptoms. This condition begins four hours after the subcutaneous injection of 0.05 c. c., and five to ten minutes after intravenous injection of 0.025 c. c. If, instead of one small injection, a series of increasing doses are given, the animal will tolerate still larger amounts. The proper vaccinating dose for man has never been determined, but subcutaneous injections of 0.5 to 2 c. c. are harmless. If, for any reason, it is feared that an injection may cause shock, it is well to precede it by one to three of these small injections. Even if disagreeable symptoms should follow, within four hours the patient would be able to tolerate a very large dose, so far as one can judge from the behavior of animals. If it is inadvisable to wait so long before an intravenous injection, one may divide the dose, giving first a minute amount, 0.1 to 0.5 c. c., and, ten minutes later, the therapeutic dose. Such a procedure is certainly no

more dangerous, and in all probability is far safer, than injecting the whole amount at once. These considerations apply only when it is desired to inject the serum directly into the circulation, or subcutaneously in large amounts, 100 to 200 c. c., as is done with certain bacteriolytic sera. They may be disregarded in the treatment of diphtheria, except in giving intravenous injections, and, for that matter, if a patient is so ill as to make an intravenous injection of diphtheria antitoxin advisable, the risk of the injection is too slight to be thought of. It should be added that unpleasant effects are much less common after the use of purified globulin preparations than when whole serum is injected. Severe reactions are less common in children than in adults.

The production of antisera in other animals than the horse has been urged in order to avoid reinjection with homologous serum, so that an individual who had previously received antidiphtheritic horse serum might in a second attack of the disease be given antidiphtheritic sheep serum. The production of such sera on a commercial scale has not yet been attempted, however.

Anaphylaxis and Intraspinal Injections.—The question of anaphylaxis after intraspinal injections of therapeutic serum requires separate consideration. It appeared at first that this practice was quite harmless, and this is certainly true of nearly all individuals. Recently, however, irritative effects of brief duration have been described by French clinicians after the injection of serum into patients with normal or chronically inflamed meninges. They believe that serum disease after intraspinal injections may take the form of a transitory serous meningitis. A few instances have also been reported of shock and even of rapid death in patients with cerebrospinal meningitis following injections made several days after the preceding dose. These cases were regarded by the observers as instances of anaphylaxis, though the time which had elapsed since the previous dose was only four or five days in most instances, and symptoms were not altogether characteristic. It seems difficult to conclude that attacks of dyspnea and convulsions occurring in a patient with meningitis are due to the action of injected serum. Certainly anaphylaxis can not be produced in this way in most individuals. The serum has often been given after a ten-day interval without any bad effects, but, in view of the possibility of anaphylactic shock occurring, such injections, if unavoidable, should be preceded by a small subcutaneous dose with an interval of a few hours (Hutinel, 74).

Treatment of Serum Disease.—The use of calcium chlorid has been recommended to prevent the urticaria, but its value is very doubtful. On the day of injection 0.5 to 1.0 gram (3 to 15 grains) may be given in divided doses to susceptible individuals, and repeated on the two following days. The same drug may also be used after the eruption has developed, and sodium salicylate in doses of 0.3 gram (5 grains) three

times a day is also recommended, though neither one is very effective. Main reliance must be placed on palliative measures to relieve the itching, such as lotions of 0.5 per cent. phenol or saturated solution of sodium bicarbonate. Some of the menthol preparations and various dusting powders have also been found useful. Adrenalin, 1-1,000, may be applied locally if the mucous membranes are involved. In cases of severe shock or syncope, stimulants should be promptly applied to increase the blood pressure. Among the most useful are adrenalin, camphor, caffein, and digitalin hypodermically. If the dyspnea is severe, atropin in doses up to 0.6 mg. (0.01 grain) may be used to relieve the bronchial spasm. In extreme cases it may occasionally be necessary to resort to artificial respiration combined with oxygen inhalations, as the respiration fails before the circulation.

Other Forms of Anaphylaxis in Man.—The tuberculin and mallein reactions are other familiar clinical examples of anaphylaxis. Attempts have been made to explain the phenomena of eclampsia, of hay fever, and of many of the food and drug rashes, on the ground of a hypersusceptibility due to previous sensitization to the toxic substance. Anaphylaxis may also bear important relations to immune therapy. The ability to react promptly and violently to the invading parasite plays a considerable part in the immunity from second attacks of the exanthemata, according to the views of von Pirquet. As an example, he believes that the resistance of a vaccinated person to smallpox may depend entirely upon allergie. If so, we have been artificially inducing this condition in our patients on empirical grounds without understanding the mechanism of the procedure. Now that so many new facts are being brought out experimentally, as shown in the excellent reviews of Anderson (2), Friedemann (53), and Besredka (13), new ways may be found of making use of this phenomenon clinically.

D. ACTIVE IMMUNIZATION—VACCINE THERAPY

The only way of stimulating the production of active immunity is by artificially producing the corresponding infection or intoxication. There is, of course, no advantage in such a procedure, unless one can eliminate the harmful effects of the disease in its spontaneous form. In the case of smallpox, for example, this can usually be done by inoculating a person in full health, the result almost always being a short, light attack. Occasionally, however, inoculated smallpox is severe; and the same end is better accomplished by producing a modified form of the disease—vaccinia—which has no dangerous features, but which confers immunity to smallpox. Similarly, in immunizing against toxins, the poison can be so weakened that it can be injected without danger, but will produce a degree of immunity which will enable the subject to withstand a stronger

dose at a second injection. The production of active immunity is called vaccination or Jennerization.

The ideal vaccine would be a form of virus or toxin which had been deprived of its poisonous properties, but retained its antigenic power. Apparently, however, the development of immunity depends, to some extent, on the same substances that produce the injury. At any rate it has never been possible entirely to remove the toxic properties from an antigenic substance. It is, however, possible so to reduce the toxic or infectious power of the vaccine that it can be used without danger and still produce immunity.

To stimulate a patient or an animal to the development of antibodies, antigen may be injected in one of several forms:

1. Fully virulent living virus (bacteria) in minute doses.
2. Attenuated virus, weakened either (a) by passage through other animals; (b) by cultivation under favorable conditions; (c) by injury through physical or chemical agents.
3. Virus killed by heat or antiseptics.
4. Extracts of virus containing no formed organisms.

We may also lessen the injurious effects by injecting any of these four forms of antigen simultaneously with the corresponding immune serum, or by treating it with the serum before injection, the product then being known as a "sensitized virus."

After inoculation or infection, the development of immunity is apparently due to the binding or destruction of the natural antibodies by the antigen and the consequent production of an excess of these substances by the organism. Active immunity, therefore, is relatively slow in its appearance and may, in some instances, be preceded by an increased susceptibility—the "negative phase" of Wright. This places a great limitation upon the use of inoculations in the treatment of disease, and it is better, where possible, to introduce preformed antibodies from an immunized animal. On the other hand, once the production of antibodies has been stimulated, the process apparently continues for a time, and the homologous antibodies are less rapidly excreted than those injected with the sera of other animals, so that an active immunity is of longer duration than is the passive type, and for this reason is preferable for prophylaxis.

Vaccination may be performed before infection, in persons who are likely to be exposed to a disease. It may also be performed after infection, during the incubation period, if the virus can be so modified that the body reacts to it more promptly than to the original form; or, finally, it may be performed after the symptoms have developed, in cases where the disease itself is not producing a sufficient reaction, but only under conditions which will prevent a temporary reduction of resistance or negative phase.

Active immunization has found a wide application in veterinary medicine, but its use in human beings is limited to those instances in which it is without danger to the individual. The most striking success has been obtained by vaccination against smallpox and rabies. Similar methods are of distinct value in the prevention of typhoid fever and plague; and in the treatment of certain chronic infections, such as furunculosis, gonorrheal arthritis, and even some forms of tuberculosis. In regard to other conditions in which vaccines have been used, experience is as yet too limited to enable one to judge of their value.

The characteristics of the vaccines and of the immunity produced will be given here, but for details of their clinical application one should refer to the chapters on the special diseases.

I. Immunization with Virulent Living Virus

The use of fully virulent virus is practically restricted to animal experimentation, though the treatment of tuberculosis with minute doses of live bacilli—beginning with a single organism—has been attempted (Webb, Williams, and Barber, 153).

II. Immunization with Attenuated Virus

1. Vaccination against Smallpox.—See Vaccination, Vol. II, Sec. I, Chapter IV.

2. Inoculation against Rabies.—See Vol. II, Sec. I, Chapter XX.

III. Immunization with Dead Organisms

1. *Theory of Method*

The risk attending the use of attenuated living virus in most infections is too great to permit the application of the method to many human diseases, though it has been employed in plague and cholera, as well as in smallpox and rabies. Injections of dead organisms are, however, comparatively safe, and for this reason it has been possible to test their value in a great variety of conditions (T. Smith, 135). These preparations are called bacterial vaccines or bacterins. They have been found useful not only in preventing the outbreak of disease, but in treating the patient after symptoms have developed. Wright introduced their use in chronic infections on the theory that the focal lesions have become so walled off from the circulation that the bacterial products are not absorbed in sufficient quantity to produce immunity, and that the bacteria introduced into the areolar tissues will incite a reaction by coming into free contact with the body fluids, thus preventing the formation of new lesions and eventually curing those already developed. This theory is supported by the phenomenon which he described as *auto-inoculation.* If a tuberculous

joint in a patient who has been free from fever is manipulated, there follow a sharp rise in temperature and increased inflammation about the affected part, closely resembling the reaction to an injection of tuberculin. Similar results can be obtained by massaging other local lesions, and Wright demonstrated by a study of the opsonic index that it was possible to produce immunity in a patient by means of these auto-inoculations. The probable explanation is that the greatly increased absorption of the products of the tubercle bacilli present in the tissues incites a reaction. It is impossible, however, to regulate the amount of toxin which will be absorbed after such a procedure, so that the method is not useful clinically. Wright also holds to the opinion that the immune bodies are formed largely in the subcutaneous tissues, and that by subcutaneous injections of vaccines, even in septicemia, a degree of immunity can be obtained greater than that produced by the bacteria in the blood stream. He has by no means succeeded in proving this latter contention, but there seems to be little doubt in regard to the success of vaccine treatment in chronic localized infections.

The immunity produced by bacterial vaccines is often restricted, not only to the species of organism used, but to the particular strain for which the vaccine is prepared. Consequently, in cases where isolation is easy enough to make such a procedure practicable, it is well to use organisms cultivated from the lesion to be treated. Where this is not practicable, it is customary to use a mixture of a number of strains of the same organism in the hope that one of these strains may be closely enough related to that causing the lesion to produce satisfactory immunity. Vaccines made from the patient's own organisms are usually referred to as *autogenous,* others as *stock vaccines.* Those made from a mixture of different strains are designated *polyvalent,* or, better, *multivalent vaccines.*

2. *Technique of Method*

a. Opsonic Index.—Wright (161) believed that bacterial immunity was due almost entirely to the presence of opsonins in the blood, and that the value of bacterial vaccines depended upon their power to stimulate an increased formation of these substances. He developed a relatively simple technique for estimating the opsonic content of a patient's serum. The organism responsible for the infection was identified and the dosage was regulated by the estimations of the opsonic index. The technique of the estimations has been severely criticized, and it is doubtful whether the opsonic strength of the blood can be accurately estimated by this method. Whatever the value of the method experimentally may be, however, clinical observations on the condition of the patient have been found more valuable as a control of vaccine therapy. The opsonic index is still followed in many cases at Wright's clinic, and by some other workers,

but is no longer generally employed. If it is desired to control treatment by this method, an estimation of the opsonic index must be made before injection and every two or three days afterward. The index before treatment will usually be below 1.0. If the vaccine is given in proper amount it will usually cause a slight lowering of the opsonic index (negative phase), which, after about two days, is followed by a rise considerably above the original point (positive phase). If no further treatment is given, this rise is followed by a gradual return to normal. A second injection should be made as near the height of the opsonic curve as possible and never during the negative phase. A satisfactory rise in the opsonic curve may occur without a preceding negative phase, but, if the increase in opsonins is only slight, it indicates that the dose was too small. On the other hand, a marked and prolonged negative phase indicates that too much vaccine was given.

The technique for determining the opsonic index and for the preparation of vaccines can be found in any textbook of clinical laboratory methods, as, for example, Wood, Chemical and Microscopical Diagnosis (160).

3. *Application of Immunization with Dead Bacteria*

Immunization with killed cultures of bacteria has been attempted for prophylaxis or therapy of the following diseases:

a. Cholera.—Prophylactic inoculation against cholera as introduced by Haffkine consisted in two injections of living vibrios, the first of an attenuated, and the second of a highly virulent, strain. Haffkine (61) found a considerable reduction in the incidence of the disease, but no reduction in mortality among the inoculated persons who became infected. The degree of protection seemed to increase during the first four days and to last about fourteen months.

Others have preferred the use of cultures killed by heat. During the Japanese epidemic of 1902, 77,907 persons were vaccinated, and the morbidity among them was 0.06 per cent., as compared with 0.13 per cent. among the uninoculated. The mortality was reduced from 75 per cent. to 42 per cent. During the latter part of the epidemic the dose of vaccine was increased, and there was no cholera among those who received the larger injections (Murata, 108).

In the Philippines Strong has used filtered extracts of agar cultures with the aim of immunizing against the endotoxins. In Bilibid prison he inoculated 1,838 persons, over one-half the inmates; and there subsequently appeared four cases of cholera among those inoculated and twenty among the uninoculated (Strong, 140).

Immunization will in no regard replace sanitary measures in repressing cholera, but it is apparently useful in regions where the disease has already broken out. Since 1896 the Indian Government has maintained a

regular station for the vaccination of coolies emigrating from infected districts in the Ganges basin, in order to prevent the spread of the disease.

b. Plague.—Immunization against plague has been extensively employed in British India. Haffkine (61), with a view to obtaining large amounts of toxin with the organisms, uses old broth cultures killed by heat. Others have advocated the use of young cultures, of a nucleoprotein prepared from pest bacilli, and of the sterilized peritoneal exudate from infected animals (natural aggressins). In the Philippines Strong (141) has employed living cultures of an atoxic strain of B. pestis. Inoculation lessens considerably the incidence of the disease, and causes a striking reduction in the mortality. It is, however, by no means as effective as general sanitary measures in restricting the spread of plague. During an epidemic in the Punjab about one-third of the population of fifty villages was inoculated with the following result (Forsyth, 50):

Classes	Number in Each	Cases of Plague	Morbidity	Number of Deaths	Mortality
Uninoculated	31,874	1,457	4.5%	659	45.2%
Inoculated	12,886	171	1.3%	29	16.9%

c. Dysentery.—Prophylactic immunization against bacillary dysentery was attempted extensively by Shiga in Japan (131). He found a diminution in the mortality among those immunized, but no reduction in morbidity. On account of the powerful endotoxins of the dysentery bacillus the reaction after injection is apt to be very severe, and unfortunately the immunity produced lasts but a short time. Combinations of bacilli and immune serum are more useful in prophylaxis of dysentery and will be mentioned later (p. 152).

d. Typhoid Fever.—The first extensive trial of prophylactic inoculations against typhoid fever was made by Wright and Leishman in India in 1898 and 1899 (162). Vaccination was also practiced in the British army during the Boer War and later in the German army during the Herero campaign in southwest Africa. Although the percentage of cases was lower than among the unvaccinated men, a number of cases of typhoid fever developed among the immunized soldiers, and the procedure fell into considerable disfavor in the British army. In 1908, however, Leishman, believing that Wright's unsatisfactory results might be due to overheating in some of the preparations, again took up the work, and by the use of suspensions killed at 53° instead of 60° C., and carefully standardized, met with much greater success. Encouraged by Leishman's report, Russell (127) has employed vaccines extensively in the United States army with most satisfactory results, very few cases of typhoid fever developing among the immunized men. Its efficacy was shown

during the army maneuvers at San Antonio in 1911. Typhoid was prevalent in that district, but among 8,000 vaccinated troops there was but one mild case. The vaccines which he uses are prepared from agar cultures sterilized at 60° C.

The immunization of hospital physicians and attendants is now practiced in many institutions. In the Massachusetts General Hospital, after two years' trial, there were no cases of undoubted house infection, although previously from two to six nurses had contracted the disease each year (Richardson, 117).

Wright and Leishman used two doses of 500 and 1,000 million respectively, with an interval of ten days. Russell gives a third dose of 1,000 million a week or ten days after the second. The injection is followed by a rather marked local reaction, and usually by a slight rise of temperature with headache and malaise. The effects are not, as a rule, severe enough to interfere with the individual's ordinary occupation. A very few cases have developed fever as high as 103° F., accompanied by chills, vomiting, and diarrhœa; but the reaction is always of short duration and no serious results have occurred. In order to prevent severe reactions, Richardson used four injections, increasing from 50 to 400 million at five-day intervals.

The agglutinins, bacteriolysins, and opsonins are much increased in the serum of the immunized individuals. There is no agreement as to the duration of the immunity produced. Often the agglutinins and opsonins return to normal in about six months; but the statistical evidence indicates that the immunity lasts somewhat longer and the period is estimated as from two to three years. The table on page 144 gives the statistical results in several large groups of cases.

These statistics seem to prove the efficacy of antityphoid vaccination, but it has been denied by Metchnikoff and Besredka on the basis of animal experiments. They were unable to protect chimpanzees against infection by injection of dead organisms, though injection of small doses of living organisms produced immunity.

The treatment of typhoid fever by vaccines was also attempted by Wright, though there seems to be little reason to expect benefit from the injection of antigens in the course of a general infection. Their use has, however, been enthusiastically advocated by some who have tried them (Watters and Eaton, 150). Improvement in symptoms following injection of vaccines has been described, and most of the reports give a slightly reduced mortality (Callison, 28). In 323 reported cases treated with vaccines there were 5.2 per cent. of deaths, as against 7 to 12 per cent. in hospital treatment; but one can hardly judge of the value of the method on the basis of so few cases. The use of typhoid vaccines has been commended in the treatment of post-typhoidal local lesions, such as periostitis, cholecystitis, and cystitis, but the number of cases is as yet

	No. of Men		Cases of Typhoid		Deaths from Typhoid		Morbidity %		Mortality %	
	Immunized	Not Inoculated	Im-munized	Not In-oculated	Im-munized	Not In-oculated	Im-munized	Not In-oculated	Im-munized	Not In-oculated
(Wright) British Army in India—1899	4,502	25,851	44	657	9	146	0.98	2.54	20.50	22.20
Garrison at Ladysmith—1900	1,705	10,259	35	1,489	8	329	2.05	14.14	22.90	22.10
(Kuhn) German Army, Southwest Africa—1904-1907	7,287	9,209	371	906	24	116	5.09	9.84	6.47	12.80
(Leishman) British Army, India—1908-1909	10,378	8,936	56	72	5	46	0.539	3.04	8.90	16.90
(Russell) United States Army—1908-1910	14,000	84,000 *circ.*	6	418	0	32	0.04	0.50	0.00	7.60

STATISTICAL RESULTS OF ANTITYPHOID VACCINATION

insufficient to determine the final value of the method. The treatment of typhoid carriers with dead bacteria has also been attempted (Irwin and Houston, 75), and, if it proves possible to free these individuals from the bacilli, a very important field for the use of vaccines will be opened up.

There is no agreement as to dosage. In most instances injections of from 25 to 100 million have been given at four or five-day intervals until defervescence begins. Some use doses of as low as two million bacilli; others give 1,000 million. Those who use the smaller doses usually repeat the injection every day or two.

The toxins of the typhoid bacillus are not set free in culture, but are contained within the cells. They may be extracted by various methods, and the extracts have been used in the treatment of the disease. Some (Hewlett and Goodall, 67) prefer them to the usual bacterins, believing that they produce an antitoxic immunity.

e. Staphylococcus Infections.—The most constantly satisfactory results obtained by the vaccine treatment have been in furunculosis. There are two groups of cases which are especially amenable to this form of treatment, and which seem to be due to an abnormally low resistance to infection by staphylococci, rather than to any unusual exposure to the infection. The first group includes those patients with recurring furuncles or carbuncles, and the second ill-nourished infants with staphylococcus skin infections. The vaccine injections in these cases occasionally have a favorable influence on the already developed lesions, but are most valuable in preventing the formation of new furuncles. Vaccines have been found valuable in acne, sycosis, impetigo, eczema, and infective dermatitis, and in pyorrhea alveolaris, though favorable results are less constant than in furunculosis (Strubell, 142). In 365 reported cases of skin infections treated with staphylococcus vaccine, 175 were cured, 154 improved, and 29 unimproved. Of these, 133 were cases of furunculosis, and 107 such were reported cured (Strubell).

The staphylococcus vaccines are also useful in otitis media, especially in subacute cases (Macdonald, 98), and in infections of the nasal sinuses when these can be shown to be due to this organism (Kolmer and Weston, 85). The use of vaccines in a series of 1,100 cases of septic rhinitis in scarlet fever resulted in 78 per cent. cures. They have been used in mastitis and various chronic wound infections.

Autogenous vaccines are more valuable than stock preparations, although both are used. The dose for adults is 50 million, increasing to 5,000 million, and given at intervals of four to five days. For infants about one-fifth of this amount is used. Vaccines should not be given during menstruation. Small doses only should be administered to diabetic patients.

f. Acne.—As staphylococcus vaccines which give fair results in pustular acne have had very little effect in cases of acne punctata, vaccines

prepared from the B. acnes (Sabouraud) have been used, and with apparent success (Fleming, 48). Small initial doses, from 3 to 10 million bacilli, are given, usually combined with staphylococcus vaccine. The organism may be cultivated on nutrient agar made acid with oleic acid, or under anaerobic conditions on neutral agar (Hartwell and Streeter, 65).

g. Gonococcus Infections.—It is generally agreed that vaccines have a favorable influence on subacute and chronic gonorrheal arthritis, and good results have also been reported from their use in epididymitis, in chronic prostatitis, and in vulvovaginitis in infants (Hamilton, 63). They have little or no influence on acute urethritis. It is more practical to use stock vaccines than to try to isolate the organism from each case; but if this is to be attempted media containing human protein, such as blood or chest serum agar, are necessary for the growth of mass cultures. The dose usually recommended is 25 to 100 million (Cole and Meakins, 36). At first large injections of 300 to 1,000 million were given with success, and some still advise the use of a dose sufficient to produce a fever of 2 to 3° F., and a distinct reaction in the focus of infection. These large injections seemed effective in a group of fifty cases of epididymitis (Bruck, 23), and, in a series of fifty-one cases of arthritis treated with smaller doses, good results were obtained in forty-two (Hartwell, 64). In vulvovaginitis doses gradually increasing from 50 to 100 million may be given at intervals of five days.

h. Streptococcus and Pneumococcus Infections.—These organisms are less often responsible for chronic infections, but nasal sinus, middle ear, and mastoid infections, and pyorrhea alveolaris due to them are frequently amenable to vaccine treatment. Good results have also been reported following their use in septicemia, acute puerperal infections, and infective endocarditis; but on the whole they have not proved useful in such conditions, nor is there theoretically any reason why they should (Watters and Eaton, 149). Horder (72) reports twelve cases of endocarditis so treated, without a recovery. In pneumonia vaccines are enthusiastically recommended by a few who have treated groups of cases with low mortality, but the same might be said of nearly every method of treating this disease. In one group of thirteen cases, mixed cultures from the patients' own sputum were used in doses of 150 to 200 million organisms. There were two deaths (Boelke, 19). Rosenow has recently reported good results from the use of large doses of autolyzed pneumococci in pneumonia. Such preparations seem to be less toxic than fresh cultures, but retain their immunizing properties.

In Russia a vaccine consisting of broth cultures of streptococci killed by heat has been extensively used in the prophylaxis of scarlatina. Three doses of from 0.5 to 2 c. c. are given at intervals of seven days. Judging from the results in communities where scarlet fever has appeared, the

vaccine confers a considerable degree of protection. The injections are frequently followed by an abrupt rise in temperature, and a scarlatiniform rash with subsequent desquamation, but this reaction does not seem to be injurious (Gabritschewsky, 55).

In treatment it is usual to begin with doses of 3 to 5 million cocci, increasing to about 100 millions. If the vaccines are used in septicemia one should be especially careful not to give too large doses, as these may be harmful.

i. **Colon Bacillus Infections.**—In a few chronic colon infections Wright obtained results which convinced him of the value of vaccines in these conditions. Chronic infections of the genitourinary tract are common, and vaccine treatment has been rather extensively tried. Dudgeon (40) treated fifty cases with only slight success, while Cabot (27) reported improvement in more than half of twenty-two cases treated, but no striking results in any. Billings (16), after rather extensive experience with vaccine therapy in these conditions, is of the opinion that symptoms are usually improved, and often very markedly so. He has observed the complete disappearance of the bacilli from the urine, but this does not often occur, even in cases which seem much benefited by the treatment. There are two difficulties in the immunization: first, the blood serum does not obtain free access to the lesion, which is usually limited to the mucous membrane; and, second, the strains of colon bacilli differ so widely in their characteristics that it is always necessary to use an autogenous vaccine. Some strains are quite toxic, and it is always well to begin with small doses of from 10 to 25 million, but the dosage may sometimes be increased rapidly to 1,000 or 5,000 million without producing marked reactions.

Vaccine in Other Infections.—A great variety of other vaccines have been introduced, but they have been used in too limited a number of cases to warrant a detailed account of each. Emulsions of dead diphtheria bacilli have been used in prophylactic immunization; and also with apparent success in a few instances in the treatment of diphtheria carriers (62). Vaccines have also been used in actinomycosis (163) and in glanders, in Malta fever (161), in influenza, and in infections with B. pyocyaneus (143), B. perfringens, Micrococcus catarrhalis (105), and the pseudodiphtheria bacillus. In whooping-cough, suspensions of the Bordet-Gengou bacillus (51) have been used; in conjunctivitis, of the Morax-Axenfeld bacillus; in asthma, of an unidentified Gram-negative bacillus (31); and patients with carcinoma have been injected with killed cultures of Micrococcus neoformans (76).

IV. Immunization with Bacterial Extracts

Immunity can be produced by the injection of the cultural products and extracts of bacterial cells which are free from intact bacteria, as was first shown by Salmon and Smith (128). The use of extracts in the prevention and treatment of disease has been recommended chiefly on the basis of two theories. The first is that these extracts contain *endotoxins.* The intoxication produced by streptococci, typhoid bacilli, cholera vibrios, and many other organisms is due to a poison which is contained in the bacterial cell, and which is not ordinarily set free in culture, in contrast to the diphtheria and tetanus bacilli, which give up to the surrounding medium large amounts of toxin (*exotoxin*). It has been thought that an antitoxic immunity against such infections might be produced by the injection of extracts which would contain endotoxins, and immune sera frequently have the power of limiting the poisonous action of this type of bacteria. It has, however, not been possible to demonstrate the existence of a true antiendotoxin which would neutralize endotoxins in definite proportions, as is true in the case of diphtheria antitoxin and toxin. The second theory is that of Bail (4), who has suggested that the power of streptococci and other organisms to invade the body depends on the secretion of substances which he calls *aggressins,* which paralyze the phagocytic activity of the host and enable infection to progress. He demonstrated the presence of these substances in the peritoneal exudates of infected animals; and by injections of such exudates into normal animals he produced an immunity which he attributed to the formation of *antiaggressins.* The same type of immunity can be produced by the injection of watery extracts of the organisms made in vitro, and such extracts have been called artificial aggressins.

The immunity produced by these soluble preparations probably does not differ essentially from that which follows the injection of bacteria. At any rate, the same immune bodies, agglutinins, lysins, tropins, etc., can usually be demonstrated in the sera. There is some evidence that they also stimulate the formation of antiendotoxins and antiaggressins, but the chief advantages of extracts are their easy absorption, their slight toxicity, and the fact that they can be sterilized by filtration and without heating. It is stated that, after injection of extracts, a longer latent period elapses before immunity appears, and that during this latent period susceptibility is somewhat increased, but this is probably true only if large doses are employed.

Immunization with extracts has been advocated in infections by a number of organisms which do not produce soluble toxins in culture, but has as yet found little clinical application. We have already mentioned the use of natural aggressins in plague and of artificial bacterial extracts

in typhoid fever and cholera. An aqueous extract of staphylococci (Histopin) has been recently introduced in treatment of skin infections. It is painted on the skin about the lesion with the view of producing a local immunity (Wassermann, 147). However, the most extensive trial of such preparations has been made in treatment of tuberculosis.

1. Tuberculin.—Neither in man nor in animals is it possible to demonstrate an immunity to tuberculosis comparable to that produced against most acute infections. A previous infection with tuberculosis or inoculation with a tuberculous vaccine may, however, render an animal intolerant of subsequent inoculation. Bacilli injected into such an animal are either walled off by rapid formation of connective tissue about them or are excreted like harmless foreign bodies. But, though a tuberculous animal is resistant to new infection, the original focus usually does not heal. The blood serum does not acquire true lytic or antitoxic properties, though agglutinins, precipitins, opsonins, and complement fixative substances (antituberculin) have been demonstrated in the serum of tuberculous men and animals. It is also possible by injections of tuberculin to make animals and man less sensitive to this substance, but such immunity, like serum antianaphylaxis, can not be transferred to other animals by injection of serum. Though vaccination of tuberculous animals, even with living attenuated bacilli, does not cure their infection, it may prevent the disease from becoming acute or generalized, and some degree of benefit may be expected from similar treatment of human beings. Dead tubercle bacilli injected intravenously produce visceral tubercles; and subcutaneously cause similar inflammatory nodules, so that active immunization in man can be attempted only with extracts.

The treatment of patients with tuberculin has been advocated on the basis of several different hypotheses. Koch originally held that he had isolated a curative principle from the bacilli which was directly beneficial. Later Wright aimed to increase the opsonins, which he thought were the natural protective substances. Both of these theories are now rather generally discarded, and it is thought that the treatment may be beneficial either by producing insusceptibility to tuberculin or by producing slight focal tuberculin reactions. It is perfectly possible to produce such insusceptibility, and those who believe that the symptoms of tuberculosis are due to poisoning with this toxin consider the procedure of great advantage to the patient. Escherich (45) has called attention to the fact that patients who are spontaneously cured of tuberculosis are not insusceptible, but hypersusceptible, to tuberculin, and he advocates, especially in infants, the use of minute and sometimes decreasing doses of tuberculin with a view to increasing rather than reducing their susceptibility.

One well known feature of the tuberculin reaction in sensitive individuals is a hyperemia and increased infiltration about the lesion. This process does not penetrate into the older caseous foci, but it seems prob-

able that an inflammatory reaction about a quiescent focus might have a distinctly beneficial effect. It is quite possible that the benefit of tuberculin treatment is due entirely to the production of such slight focal reactions. Any marked reaction, however, may be distinctly harmful and should be carefully avoided.

Whatever may be the mechanism by which tuberculin acts, it is apparently of real clinical value in certain cases. Those which are most amenable to treatment are the well localized and quiescent infections, such as tuberculosis of the bones, joints, and lymph nodes (Nutt and Hastings, 111). It is sometimes beneficial in ocular (Junius, 79) and in genitourinary tuberculosis and in lupus (Carmalt-Jones, 30), though it is hardly to be recommended in cases where operative removal of the lesion is possible. Pulmonary lesions which are inactive, as shown by the absence of continuous fever, are also amenable to treatment (Baldwin, 5). Its use in more active cases is generally viewed with disfavor, but Löwenstein (96) reports its use in 682 such cases, in 53 per cent. of which the bacilli disappeared from the sputum.

Since the appearance of Koch's original tuberculin, an immense variety of preparations has been produced, for each of which special advantages are claimed. These fall into two main groups: first, the soluble metabolic products of the tubercle bacillus as produced in fluid culture; and, second, extracts and emulsions of the bacilli made by mechanical trituration, or by chemical extraction. The first group probably also contains some of the cell constituents set free by autolysis.

Koch's original tuberculin (81) consists of cultures in glycerin bouillon from six to eight weeks old, concentrated to one-tenth their volume at 100° C., and filtered free from bacteria. In order to avoid injury to the toxins by heat, Denys (38) introduced his bouillon filtré (B F), which consists of similar cultures unconcentrated and sterilized by passage through a Chamberland filter. The vacuum tuberculin consists of filtered bouillon concentrated to one-tenth its original volume in vacuo at a low temperature.

The type of emulsions of the bacillary bodies is Koch's new tuberculin. Virulent young cultures are dried in vacuo and ground until practically no stainable tubercle bacilli remain. They are then extracted with distilled water, and the insoluble portion separated by centrifugalization. This first extract, called T O, is similar in its action to old tuberculin. The sediment is then emulsified by repeated trituration and extraction and centrifugalization until practically no residue is left. The clear opalescent fluid thus obtained is called T R (82). It is precipitated by 50 per cent. glycerin, in distinction to T O, which is soluble. It is less apt to produce a reaction, and Koch regarded its action as almost exclusively immunizing. T R as sold contains about 20 per cent. glycerin as a preservative. Phenol, which is used in the old tuberculin,

is not suitable and should not be employed in making dilutions. As originally prepared by Koch, T R contained 10 mg. of solid matter to the c. c. Some preparations now sold are more dilute. Later Koch introduced a combination of T O and T R under the name of bacillary emulsion (B E) (83). It consists of the ground bacilli suspended in 50 per cent. glycerin, from which the coarser particles are removed by sedimentation. It contains 5 mg. of dried substance to the c. c.

Among the extracts of tubercle bacilli may be mentioned tuberculoplasmin, an extract prepared by subjecting the bacilli to a pressure of 400 atmospheres (Büchner and Hahn, 24). Another well known preparation is Landmann's tuberculole (90), of which there are three forms. Tuberculole B is made by freeing the dried bacilli from fat, grinding them, and extracting the powder three times with dilute glycerin, first at 40°, then at 50°, and then at 100°, and concentrating the combined extracts in a vacuum at 37° C. Tuberculole C is the filtered bouillon, likewise concentrated at 37° C.; and Tuberculole A is a mixture of B and C. Béraneck's tuberculin (12) is prepared from cultures grown in acid 5 per cent. glycerin bouillon, an extract of bacilli made with 1 per cent. phosphoric acid being added to the filtered bouillon. It is said to have very slight toxicity. Von Ruck (124) has prepared a "watery extract of tubercle bacilli." Tuberculin purum or endotin is a preparation made by freeing the bacilli from fatty substances by extraction with xylol, ether, chloroform, and alcohol. This, it is claimed, is a harmless substance, but it is also apparently very weak in specific properties (Vos, B. H., 146). Tebean is a recent preparation (92), in which the tubercle bacilli are killed with 24 per cent. galactose solution. It is not to be recommended, as in some instances abscesses have appeared at the site of injection. Von Behring (10) in 1907 introduced his Tulase, an alkaline suspension of tubercle bacilli killed with chloral hydrate. This also proved very irritating and has been withdrawn from the market. In 1891 Klebs (80) introduced Tuberculocidin, made by precipitating tuberculin with alcohol and bismuth; and Calmette (29) has prepared an alcohol precipitate from cultures of bovine tubercle bacilli, under the name of C L. The initial dose is 0.001 mg. Rosenbach (122) has prepared a tuberculin by mixing tubercle bacilli with a trichophyton, with the aim of reducing the toxicity. Deycke and Much (39), having the same object in view, have introduced a mixture of tuberculin with human brain. They have also extracted a fatty substance, nastin, from a saprophytic streptothrix, which they consider to be chemically identical with the fatty constituent of the tubercle bacillus, tuberculo-nastin.

Bovine tubercle bacilli are less infectious to man than human strains, and Spengler (139) has advocated the use of a bouillon filtré prepared from these bacilli (Perlsucht tuberculin, P T O); and also of an emul-

sion of bovine bacilli prepared in the same way as Koch's new tuberculin (B E).

Attempts have also been made to use autogenous tuberculins (Briscoe and Williams, 22); and a mixed tuberculin from various strains of bacilli has been prepared (Rothschild, 123).

None of these modifications has proved essentially better than the original preparations of Koch, and the result of treatment apparently depends more upon careful dosage than upon the particular preparation used. It would seem that the emulsions would be more likely to produce immunity than the filtered cultures, but no true immunity can be demonstrated after use of either. The broth filtrates are more apt to produce reactions, but they have the advantage of being easily absorbed and therefore more constant in their effects.

In respect to dosage, the chief care should be to avoid producing a systemic reaction. If one aims to produce minimal focal reactions, the amount of successive doses should be increased very slightly, or even diminished. If, on the other hand, it be desired to produce an insusceptibility to tuberculin, the dose may be doubled each time, provided no reaction has resulted from the previous injection. With old tuberculin it is customary to begin with 0.01 or 0.12 mg. (or more strictly 0.01 to 0.12 cu. mm.). Some increase this up to 1,000 mg.; others regard 1 mg. as the maximum. The corresponding dose of new tuberculin, B E or T R, and of bouillon filtré, is one-tenth or one-twentieth of this amount. The injections should be made subcutaneously.

2. **Trichophytin.**—Patients with certain deep infections with ringworm fungi give a local and general reaction after injections with extracts of the fungus, similar to the tuberculin reaction. Only certain cultures seem capable of producing this reaction. Excellent results have been obtained in deep infections by single injections of filtered bouillon in which the fungi had grown for several months. The ordinary superficial infections are only slightly influenced by these injections (Kusunoki, 88).

V. Combination Methods

Sero-vaccination—Sensitized Vaccines

Prophylactic immunization by simultaneous injections of virus and immune serum has found extensive application in veterinary medicine, and has proved successful in the control of cattle plague, swine erysipelas, and other epizoötic diseases. This procedure, known as *sero-vaccination,* was introduced in Japan in 1900 for the control of bacillary dysentery in man (Shiga, 132). The dead bacilli alone are very toxic, but it was found that their effect could be diminished by simultaneous injections of

small amounts of immune serum. The combined inoculations did not markedly reduce the incidence of the disease, but lowered the mortality from 30 or 40 per cent. to nearly zero. The same method has been used quite recently to protect infants from summer diarrhea with only slight success; two fatal cases occurred in a series of ninety-five vaccinated infants (Lucas and Amoss, 97). Streptococcus vaccine in combination with antistreptococcus serum has been recommended in septicemia, and good results are reported following their use in scarlet fever (Jochmann and Michaelis, 78). Vaccine and immune serum have also been used simultaneously in pneumonia.

If too much of the protective serum is used in such injections, very slight immunity is produced. Consequently it has been proposed to treat the bacteria with immune serum in vitro, and then wash them free from excess of antibodies by centrifugalization. Such sensitized vaccines cause relatively slight reaction when injected into laboratory animals, but produce immunity more rapidly than the dead bacteria alone (Besredka, 14). Practical application of this method has been made in antirabic inoculations, and a sensitized vaccine for use in tuberculosis has been prepared by treating ground bacilli with immune serum. The use of similar vaccines has been advocated for immunizing against the dysentery bacillus and other organisms which contain powerful endotoxins, but they have not yet been tried out clinically. In the prophylaxis of diphtheria also, Theobald Smith (134) has recommended injections of toxin combined with a neutralizing dose of antitoxin which would give a much more durable protection than the immune serum alone.

E. PASSIVE IMMUNIZATION—SERUM THERAPY

Passive immunity is, in contrast to the types just considered, characterized by its rapid appearance and short duration. When serum is injected subcutaneously, the antibodies reach their maximum in the circulation in from twenty-four to seventy-two hours, large amounts requiring the longer time for their absorption. The greatest concentration is obtained almost immediately when serum is introduced directly into the veins. On the other hand, the exogenous antibodies are quickly eliminated from the body, and the curve of resistance rises abruptly to a maximum and falls much more rapidly than in active immunization.

It has been the ideal of experimenters to perfect bactericidal sera—i. e., those which would destroy the parasites directly; but better practical results have been obtained with sera which neutralize their poisonous products—antitoxic sera. For prophylaxis we may passively immunize normal individuals, but the protection conferred is of such short duration that this procedure has few applications, and is limited to the control

of epidemics and the protection of physicians and hospital attendants. The best results with passive immunization are obtained by injections during the incubation period; these frequently prevent the development of the disease. After the symptoms have appeared we may hope, by the use of sera, to eliminate the infecting parasite or neutralize the toxins which it produces. After injections of immune serum there is no negative phase and little or no latent period, consequently this method has a great advantage over active immunization in the treatment of disease.

There are three diseases in which passive immunization has proved of undoubted value—diphtheria, tetanus, and epidemic meningitis. Other immune sera, the value of which is less well established, will, however, be briefly mentioned. A number of other sera have been tried clinically, such as anti-Malta fever serum, antirabic serum, etc., which have not proved of the least importance, and will, in consequence, be omitted from the following pages.

I. Antitoxic Sera

a. *Diphtheria Antitoxin*

By far the most successful clinical application of immunity has been in the treatment of diphtheria with antitoxin. Diphtheria is characterized by a local superficial infection with the diphtheria bacilli, usually on the tonsils, and a general intoxication caused by absorption of their poisonous products. The bacilli themselves sometimes gain access to the circulation, but the toxin can always be demonstrated in the blood and frequently causes degenerative changes in the heart, kidneys, and peripheral nerves. This same toxin is secreted by the bacilli when they are grown on artificial media, and it is possible to produce all the symptoms of an infection in animals by the injection of filtered cultures freed from bacilli. The toxin acts after a latent period of about 24 hours.

Nature of the Toxin.—The chemical nature of this poison is not known. It is precipitated by alcohol and by saturation of the culture fluid with ammonium sulphate, but preparations have been made which are not coagulated by heat and do not give the usual reactions of protein. It is quite unstable, being promptly destroyed by boiling and by exposure to 73° C. for 5 minutes, and injured by freezing and the action of light. It is an extremely powerful poison, and 0.005 c. c. of an active culture filtrate is fatal to a guinea-pig.

Preparation of the Toxin.—Different strains of bacilli vary greatly in the amount of toxin which they secrete in culture, and the nature of the medium on which they are grown also influences the production. For practical purposes a particular strain, known as the Park-Williams Bacillus No. 8, is very widely used, as this has maintained its remarkable

toxin-producing qualities after seventeen years of cultivation. The amount of toxin in a culture rises to a maximum in about one week, and then gradually diminishes on account of autolytic processes. The bacilli are cultivated in broad flasks containing a shallow layer of weakly alkaline bouillon with at least 2 per cent. of peptone. After a week's incubation the culture is sterilized by adding 0.5 per cent. of phenol. The dead bacilli soon settle out, and the broth containing the toxin is siphoned off and filtered.

Nature of the Antitoxin.—The serum of animals immunized against diphtheria toxin contains a typical antitoxin, which completely neutralizes the toxin when mixed with it in vitro, or when injected into animals before or immediately after an injection of toxin. The antitoxin is carried down when the pseudoglobulins of the serum are precipitated and may have the same chemical characteristics except in its resistance to heat. It is only slightly affected by a temperature of 56° C., but is promptly destroyed by exposure to a temperature of 60° C. By injections of washed diphtheria bacilli, sera can be produced which contain agglutinins, lysins, and substances which neutralize the toxic action of the bacterial cells, but these bodies are not present in any considerable amount in the therapeutic sera. Bacteriolysins and agglutinins can be demonstrated in some preparations, but not in most. Antitoxin introduced intravenously or subcutaneously can be demonstrated in the blood serum for a period of two or three weeks. Injected into the body of a diphtheria patient, it combines with the toxins circulating in the blood with consequent disappearance of the symptoms which these produce. It has a marked effect on the local lesion also, the injections usually being followed by a demarcation and prompt sloughing of the membrane. Injections of serum have a more marked effect than local applications of antiseptics, and in cases of laryngeal diphtheria this influence on the membrane may be much more beneficial to the patient than the purely antitoxic action. Closely related to its action on the membrane is the power of antitoxin to prevent infection when injected into normal individuals. The mechanism of this action has never been demonstrated. It is probably not directly bactericidal, as the antidiphtheritic serum usually forms a good culture medium for the bacilli. Some claim that this antibacterial action is dependent on an immune opsonin in the serum which depends for its activity on the presence of fresh complement. It may be that the growth of the bacilli in the body depends on the production of aggressins which prevent phagocytosis, and which are neutralized by the serum.

The Preparation of Antitoxin.—The production of a satisfactory antitoxin requires considerable skill and experience. Young healthy horses are used for immunization. It is best to use a very strong toxin, which for the first injections is weakened, either by the addition of some chem-

ical agent, or by combination with antitoxin. The first injection may consist of 5,000 units of toxin combined with 10,000 units of antitoxin, and this may be followed by injections of toxin alone at three-day intervals. The amount is gradually increased to about 300,000 units of toxin at the end of two months. If the serum is then of suitable strength, the horses are bled every week and are also given an increased dose of toxin weekly. Some horses never attain a satisfactory immunity, and only about 10 per cent. develop as much as 800 units in 1 c. c. of serum. The blood is drawn from the jugular vein and received in jars or Erlenmeyer flasks, in which it is stored for four days to permit separation of the serum. The serum is then drawn off and usually stored for some time in the cold, as when absolutely fresh it is more apt to produce a rash. If kept at room temperature it loses about twenty per cent. of its strength in a year, but at 5° C. it is reduced only six per cent. in the same time. In most laboratories a preservative, either 0.4 per cent. tricresol or 0.5 per cent. phenol, is added; but this is not necessary.

Concentration of Antitoxin.—The unpleasant and even harmful results which have sometimes followed injections of horse serum are due not to the antitoxin, but to normal constituents of the serum. Consequently, in many laboratories the antitoxin is freed, as far as possible, from other forms of protein, and such preparations are known as concentrated antitoxin or immune globulins. Banzhaf (6) has perfected the following method which is used in the laboratories of the New York City Department of Health: The blood is received directly into a citrate solution, and the blood cells removed by sedimentation. The plasma is then heated to 56° C. for twelve hours, which converts about one-third of the pseudoglobulin into euglobulin without diminishing the antitoxin content by more than 5 per cent. The euglobulins are then removed by one-third saturation with ammonium sulphate and the pseudoglobulins containing the antitoxin precipitated from the filtrate by adding ammonium sulphate to 54 per cent. saturation. Some of the pseudoglobulin which is brought down in the first precipitation is recovered by extracting the euglobulin precipitate with saturated sodium chlorid, and is again precipitated from this solution with dilute acetic acid. The precipitates are freed from excess of fluid by pressure and dialyzed in parchment paper for one week against running tap water to remove the excess of salts. They are then filtered through paper pulp and finally through a Berkefeld filter to remove foreign bodies and bacteria. This concentrated preparation contains about 80 per cent. more antitoxin per unit volume than the original serum. In practice it produces fewer symptoms of serum disease than the whole serum, a result which is due partly to the removal of the non-antitoxic protein, and doubtless also to the fact that the heating of serum diminishes its power to produce anaphylactic shock.

Standardization of Antitoxin.—The unit of diphtheria toxin was originally defined as the amount just sufficient to kill a guinea-pig of 250 grams in four days, and the unit of antitoxin as the amount which will just neutralize 100 units of toxin (Rosenau, 120).

The standardization is rendered difficult by the fact that filtered cultures contain substances known as toxoids, which are non-poisonous, but which have the power of neutralizing antitoxin. Consequently, the ratio between the lethal dose of a toxin and its power to neutralize an antitoxin is not constant. The antitoxin, however, is more uniform in its composition, and is used as the standard. In this country all toxins are tested by comparison with a standard antitoxin preserved at the laboratories of the Public Health Service in Washington, the unit value of which is arbitrarily defined, but corresponds roughly to that given by the original method of determination. To determine the strength of a toxic broth, graded amounts of it are mixed with 1 unit of standard antitoxin and injected into a series of guinea-pigs. The largest amount administered to a pig which survives for four days is regarded as the test dose. An immune serum is tested by mixing graded amounts of it each with a test dose of the carefully standardized toxin, and injecting the mixtures into a series of guinea-pigs. The smallest amount which suffices to protect the animal for four days is regarded as the unit.

Administration of Antitoxin.—See Vol. II, Sec. I, Chapter XIV.

Value of Antitoxin.—There are those who dispute the value of diphtheria antitoxin, though a careful review of the various statistics leads to the conclusion that it has reduced the mortality at least 50 per cent. During the ten years after antitoxin was first generally used the mortality from diphtheria in New York City fell from 158 to 36 per hundred thousand (Park, 112). The results are more favorable in cases injected early in the course of the disease, as is shown by the following tabulation of 9,581 cases in which the total mortality was 15.5 per cent.:

Day of injection,	1st	2d	3d	4th	5th	Later
Mortality........	6.6	8.3	12.9	17.0	23.2	26.9 per cent.

The effect of the serum on the membrane has lessened greatly the mortality from laryngeal diphtheria. Very large injections are said to be of value also in post-diphtheritic paralyses, and certainly the early injection of antitoxin lessens the frequency and severity of these sequelæ.

A prophylactic injection is usually, but not invariably, effective. It confers almost absolute protection for two weeks after injection, after which its influence gradually diminishes. The prophylactic value of the antitoxin has been shown in the protection of physicians, nurses, and those exposed during epidemics, but, doubtless, owing to the short duration of the immunity induced, it has not caused a marked reduction in

the prevalence of the disease. For a more detailed discussion of immunity in diphtheria the reader is referred to v. Behring's book in the Bibliothek von Coler (9).

b. Tetanus Antitoxin

Tetanus, like diphtheria, is a disease produced by toxins secreted by bacteria which grow only in a local lesion. The toxin is also formed in cultures, and when injected into animals produces all the symptoms of tetanus after an incubation period of two to three days. The toxin has never been isolated, but its characteristics are similar to those of diphtheria toxin, and it is apparently not a true protein. It is far more powerful than diphtheria toxin, and in its purest form 0.00005 mg. is fatal to a mouse. In fluid form it is very labile, but in dried form and protected from light and moisture it is much more resistant. If precipitated by saturating the filtered broth with ammonium sulphate and dried over sulphuric acid, it preserves its strength indefinitely.

Tetanus bacilli have no injurious effect of themselves, and if introduced into the body without foreign bodies or free toxin they do not secrete any toxin and apparently become the prey of leukocytes. This may explain in part the protective action of antitoxic serum, for, if the bacilli are protected from the leukocytes by a paper sac, they multiply even in an immune animal.

The bacilli secrete two toxins. One, tetanolysin, has the power of laking red blood cells, but it is doubtful if this plays any part in the disease. The other, tetanospasmin, has a specific action on the ganglion cells of the central nervous system, and it produces no effects until combined with these cells. The toxin has an affinity for the lipoid substances of the brain which neutralize it in vitro. It quickly appears in the circulating blood of infected animals, but reaches the spinal cord only by passage up the nerve trunks; according to some, through the axis cylinders; according to others, through the perineural lymph spaces. It may reach the cord through the nerves leading to the seat of infection, in which case the spasm begins in that region, or it may, through the blood stream, reach nerves in other parts of the body and so pass to the central nervous system. The spasm then frequently begins in the muscles of the jaw, as the nerves supplying these are very short and transmit the toxin quickly to the motor ganglia.

Production of the Antitoxin.—For use in immunization the toxin is produced by cultivating the bacilli anaerobically in weakly alkaline media. Ordinary broth made with fresh meat infusion is quite suitable, though a variety of substances are added in some laboratories to favor toxin production. The bacilli may also be grown in aerobic cultures in symbiosis with B. subtilis and other organisms. The filtrate of a six to ten days' culture is used for immunization.

The antitoxin has the power of neutralizing toxin if combined with it in vitro or in the serum of living animals, but not after it has become attached to the cells of the central nervous system. It has the same chemical properties as diphtheria antitoxin. Some of the therapeutic sera contain agglutinins, but none show specific complement-binding substances (Schurmann, 130).

In the production of tetanus antitoxin for therapeutic use healthy young horses are employed. The toxin is usually weakened for the first injections by combination with iodin terchlorid or other chemical agents; but one may begin with 3,000 units or more of full strength toxin combined with twice the neutralizing amount of antitoxin. The injections are given several days apart until the animals tolerate 500,000 to 600,000 units. In the Swiss Serum Institute whole cultures containing spores and bacilli are used, instead of filtrate. The general technique for injecting the toxin and obtaining the serum is the same as that for producing diphtheria antitoxin, and the antitetanic serum may to advantage be concentrated in exactly the same manner.

Standardization of the Antitoxin.—The unit of tetanus toxin adopted in this country is that amount which is just sufficient to kill a 350-gram guinea-pig. A standard toxin is kept by the United States Public Health and Marine Hospital Service in Washington, and is furnished free for standardization purposes. The unit of antitoxin is ten times the amount which will protect a 350-gram guinea-pig for ninety-six hours against one official dose of toxin, 100 units (Rosenau and Anderson, 121). The German unit is much larger (about seventy-five times) and is determined by a method which gives less constant results.

Administration of the Antitoxin.—See Vol. II, Sec. I, Chapter XXI.

c. *Antitoxin against Snake Venom or Antivenin*

Snake venom contains a number of separate toxins of which a neurotoxin, acting on the motor nerve cells, an hemorrhagin, acting on the endothelium of blood vessels, an hemolysin, acting on the red blood cells, and a body resembling fibrin ferment, have been identified (Willson, 157). Different venoms vary widely in their composition. Those of the poisonous Colubrines, of which the cobras are the chief representatives, and the coral snake, the only species in this country, all contain large amounts of neurotoxin. Death from the bites of these snakes is due almost entirely to the paralyzing action of this poison on the pneumogastric center. It also has a curare-like action on the nerve endings. The Viperines, to which group the rattlesnake, the water moccasin, and the copper-head belong, secrete a venom which contains only small amounts of neurotoxin and large quantities of hemorrhagin and of fibrin ferment. It causes severe edema, hemorrhage, and necrosis in the region of the punc-

ture, and its paralyzing action on the spinal cord may be the result of thrombosis (Noguchi, 110).

Animals injected with sublethal doses acquire an immunity to venom, due to the development of antitoxin in their blood. Their serum neutralizes the corresponding venom in vitro, often with the formation of a precipitate, and confers passive immunity when injected into another animal. The antibodies are usually specific for the venom of each genus of snake, and those binding neurotoxin are distinct from those neutralizing hemorrhagin.

The harmless combination of toxin and antitoxin may be broken up by heat, or by chemical agents to which the antitoxin is sensitive and the venom resistant, with a restoration of the toxic power of the mixture. This shows that the antibody does not break down the toxin, but binds it in a way which prevents combination with the body cells.

The production of antivenins powerful enough for clinical purposes is very difficult. Calmette has prepared an antitoxin for cobra venom which is sold as "sérum antivenimeux," of which 700 c. c. would be required to neutralize the maximum amount of venom which a cobra could inject (Lamb, 89). Nevertheless, good results have been reported from the use of relatively small amounts, 10 to 20 c. c. This serum is of no value against viper bites, but in Brazil a polyvalent serum has been prepared by immunization against the venom of several different species of viperines, and in Japan a trimeresurus antivenin has been used with considerable success. The value of the treatment is limited by the difficulty of having the serum at hand when it is needed, and as yet no serum has been produced which is powerful enough to insure recovery in all cases.

d. Pollantin

Dunbar attributes the symptoms of hay fever to the toxins in certain pollens which are able to penetrate the mucous membrane of individuals who, on account of vasomotor instability or for other reasons, are susceptible. The type of the disease occurring in America appears in the fall and is due to the pollen of the Solidagineæ (goldenrods) and Ambrosiaceæ (ragweed). In Germany the disease occurs earlier and is due to the pollen of grasses and grains (Gramineæ). Dunbar describes an analogous malady in China due to the pollen of the Ligusticum vulgare. He does not regard it as a strictly anaphylactic reaction, but has obtained anaphylactic symptoms in guinea-pigs by injecting the sera of hay fever patients in combination with pollen proteid. Pollen proteid applied to the conjunctiva of a susceptible individual produces a typical local reaction at any time.

In 1903 Dunbar (42) brought out a serum prepared by immunizing horses to pollen proteid. This pollantin in liquid or powdered form is

applied to the conjunctiva or nasal mucous membrane of the patient. Subcutaneously it has no effect, but Dunbar and others claim that, if used before the mucosa is so swollen as to interfere with absorption, it will prevent an attack, and that, if attacks are warded off for some time, the individual gradually becomes insusceptible. For those to whom horse serum is irritating a special powder marked "R" which contains a large proportion of lactose is used.

e. *Graminol*

Assuming that ruminants would become immune to the toxin of the pollens, Weichardt (154) has introduced the use of their dried serum under the name of Graminol as a cure for hay fever.

f. *Meat Poisoning*

The B. botulinus, which is very often found to be the cause of meat poisoning in Europe, produces a very powerful soluble toxin. A specific antitoxin, which is efficient as tested in laboratory animals, has been prepared by the Berlin Institute for Infectious Diseases, but its clinical value has not been demonstrated (Madsen, 100).

II. Bactericidal Sera

a. *Antimeningococcus Serum*

For some years it has been known that immune serum would protect animals against meningococci. In 1906 Jochmann (77) and Wassermann and Kolle (148) reported the treatment of patients by subcutaneous and occasionally by intraspinal injections of an antimeningococcus serum, with results which were somewhat encouraging. A more distinct success was obtained by Flexner, who in 1908 brought out a serum prepared by immunizing horses, and reported its use in forty-seven cases with a mortality of 27.6 per cent. (49).* His method of preparation did not differ radically from that of other workers, and his success was due largely to the exclusive use of injection by lumbar puncture. Flexner adopted this procedure on account of the "advantage of bringing the antiserum into direct contact with the focus of infection" and "the knowledge that elimination of colloids from the blood stream into the cerebrospinal fluid is a slow and imperfect process." The serum is now extensively used.

The Flexner serum is prepared by injecting horses subcutaneously, first with dead, and later with living, cultures of meningococci. Between

*See also the chapter on Cerebrospinal Meningitis, Vol. II, Sec. I, Chapter XII.

each two injections, the animal is given a dose of autolysate, prepared by digesting agar cultures with salt solution under toluol. The immunization is continued from four to six months, until the animals tolerate enormous doses of the extract.

The Wassermann and Kolle serum is a mixture obtained from three horses, the first immunized by subcutaneous injections of dead and living cultures, the second immunized by similar intravenous injections, the third immunized against distilled water extracts of the cultures. Other sera are prepared by use of cocci alone, dispensing with extracts.

The sera contain agglutinins, precipitins, bactericidal, bacteriotropic, and complement-binding substances. They are also antiendotoxic, or at least exhibit a protective action in animals against injections of dead cocci. The bacterial extracts are used in immunization with a view to increasing their antitoxic power and preventing injury from the endotoxins set free by lytic bodies in the serum.

The standardization of meningococcus antisera is difficult on account of the inconstant pathogenicity of the cocci. Flexner regards the bacteriotropic content as the best index of their strength, and uses a modification of Neufeld's technique in standardization. Wassermann and Kolle use the complement deviation method, and others test the protective action of the serum in small laboratory animals.

The effect of the serum is due, according to Flexner, to three factors: the direct bactericidal action, the stimulation of phagocytosis, and the neutralization of free toxins. It is shown by a prompt reduction of the number of cocci in the exudate, the extracellular forms practically disappearing, and the failure of the remaining cocci to grow in culture. After injection of serum, the exudate becomes less purulent, the leukocytosis of the blood falls, and in about 25 per cent. of the successfully treated cases the temperature drops by crisis.

Administration.—See Vol. II, Sec. I, Chapter XII.

b. *Antiinfluenza Serum*

The successful employment of the serum treatment in cases of meningitis due to infection with the meningococcus has led to attempts to develop a similar treatment for the form of the disease produced by the influenza bacillus (Wollstein, 159). The serum is obtained by treating goats for a long period with living cultures of the bacilli. It contains agglutinins and opsonins, but no bacteriolytic substances. It has proved useful in experimental meningitis in monkeys, but there are as yet no reports of its therapeutic use in human beings.

c. *Antistreptococcus Serum*

Attempts to obtain an antiserum for use in streptococcus infections were made by von Behring and others immediately after the successful employment of serum treatment in diphtheria, but up to the present time these attempts have not yielded very satisfactory results. Aside from the difficulties in immunizing against any organism which acts by means of an endotoxin, the great biological differences existing between the various strains of streptococci make it hard to obtain a serum which is generally applicable. Most of the sera now in use either are advocated for one class of streptococcus infections, such as rheumatism or scarlatinal angina, or are made polyvalent by the use of a number of different types of organisms in the immunization. Some workers advocate the use of cultures whose virulence has been greatly increased by passage through animals; others assert that only cocci recently isolated from human lesions should be used. The best known method is that of Aronson (3), which consists in obtaining a basic immunity in a horse, by injections of increasing doses of a culture of artificially exalted virulence. After a satisfactory immunity is obtained, the serum is made polyvalent by injecting the animal with a number of freshly isolated organisms.

The Meyer-Ruppel (107) serum is a mixture of the sera obtained from several horses, each immunized to cocci of a different origin. Avirulent strains are passed through a number of small animals and are used for the first injections; later, original cultures preserved in defibrinated blood are used. Each of the component sera is standardized separately by testing its power to protect animals against the corresponding strain of streptococci. Aronson's serum is tested only against the one highly virulent strain. A serum, 1 c. c. of which will protect a mouse against 100 lethal doses, he calls normal, and recommends for use a twenty-times normal serum. In some laboratories serum is tested merely by clinical observation.

Antistreptococcus serum contains agglutinins and bactericidal bodies, but its beneficial action depends chiefly upon the bacteriotropins. Examinations of five sera on sale in this country showed four to be active and one inactive (Weaver and Tunnicliff, 152). Injected into guinea-pigs, they showed a protective action against subsequent injections of streptococci, but no curative action on a previous infection. Bacteriotropins could be demonstrated in vitro only if the sera were quite fresh; but the tropic power of moderately old sera could be restored by reactivation with fresh human serum. Such reactivation would doubtless take place if the commercial sera were injected into patients.

These sera have been tried in all varieties of streptococcus infections. In erysipelas they have been usually unsuccessful. In puerperal sepsis (Bumm, 26) and septicemias following trauma they appear to be of some

value, though the results are far from uniform. The best results are obtained by those who inject early in the disease without waiting for a positive blood culture, and this would seem the most promising procedure, though it is difficult to draw conclusions from such cases on account of the uncertainty of the diagnosis. Polyvalent sera and Moser's scarlatina serum (Bukowsky, 25) have been used extensively in severe scarlatinas, especially those complicated by angina or streptococcus septicemia. Nicoll (109a) on the basis of his experience in thirty cases of scarlatina recommends large injections in all severe infections, the dosage being 200 c. c. for older children and adults. Most of the reports from the Russian and Austrian clinics are favorable. but the results attained elsewhere have been less encouraging.

A special serum has been prepared for the treatment of chronic and acute articular rheumatism (Menzer, 105), which seems of rather doubtful value. Cases of ulcerative and vegetative endocarditis seem less amenable to treatment than other types of septicemia, and harmful results have been reported following large doses, due perhaps to a local reaction set up at the site of the valvular lesion. It is well to restrict the serum treatment in these conditions to small subcutaneous injections. In general infections the serum is used subcutaneously in doses of from 10 to 50 c. c., and in scarlatina in doses of from 100 to 200 c. c. The results of intravenous injections of from 20 to 50 c. c. are usually more striking. The serum is used locally in packing wounds and in dried form for insufflations in angina. In peritonitis it has been introduced directly into the peritoneum in amounts up to 100 c. c., usually diluted with salt solution; and 20 to 40 c. c. may be injected by lumbar puncture in meningitis. Prophylactically it is used in some clinics before major obstetrical operations, and also in scarlatina, with a view to preventing complications. In chronic infections or for prophylaxis, injections of the serum may be combined with streptococcus vaccines.

The results seem to justify the use of the serum in puerperal infections, preferably while the infection is still confined to the uterus, and in streptococcal wound infections or peritonitis, whether a septicemia can be demonstrated or not.

d. Antipneumococcus Serum

Various attempts have been made to produce an effective serum for use in pneumonia and other pneumococcus infections. Römer (119) has prepared a mixed serum from several species of animals by injecting horses, cattle, and sheep with numerous strains of pneumococci freshly isolated from the human body. The serum contains agglutinins, precipitins, and bactericidal and bacteriotropic substances, and Römer thinks also an antitoxic product. He reports success in the treatment of ulcus

serpens. Others conclude that pneumonia runs a milder course under the treatment with the serum, and that the pneumococci disappear from the blood (Pässler, 113). The majority of clinicians, however, do not seem to be convinced of its value. Merck dispenses a similar polyvalent serum. It is standardized so that 1/100 of an antitoxin unit will protect a mouse against 10 to 100 lethal doses of pneumococci.

In infections of the eye some drop the serum into the conjunctival sack, but Römer uses from 10 to 100 c. c. subcutaneously, and he thinks that the frequent failure of the serum is due to the use of too small doses. In treatment of pneumonia he recommends large intravenous injections diluted with salt solution. The usual dose is 10 to 20 c. c. for adults, and 5 to 10 c. c. for children.

e. *Antigonococcus Serum*

In the serum of animals immunized to gonococci Torrey has demonstrated agglutinins, precipitins, and bactericidal and complement fixative bodies. Rogers and Torrey (118) have introduced a polyvalent serum prepared by immunizing rams by intraperitoneal injections of several strains of gonococci, which differ in their agglutinative properties. The serum is standardized by agglutination tests.

A number of clinicians report the successful use of the serum in gonorrheal infections of the joints and tendon sheaths, and to some extent in subacute or chronic urethritis and epididymitis (Thomas, 143). They agree that it is without effect in acute conjunctivitis and urethritis. The dose is 2 c. c. subcutaneously every two days. The injections usually cause a temporary reaction in the lesion.

f. *Antidysenteric Serum*

In bacillary dysentery the bacilli multiply almost exclusively in the intestinal tract and are very slightly affected by immune bodies in the serum of the patients. On the other hand, the symptoms in severe cases are due largely to the absorption of toxins into the circulation. The Shiga type of dysentery bacillus produces a soluble toxin in culture, to which horses are very sensitive.

Very good results are reported from European clinics following the use of an antitoxic serum in the severer types of dysentery (Skschivan and Stefansky, 133). Injections of from 10 to 60 c. c. are given subcutaneously every two or three days. In America the disease is usually due to the Flexner type of bacillus, which does not produce a soluble toxin. This makes the production of a satisfactory serum more difficult, but encouraging results have been obtained with a serum of horses immunized

to dead cultures of this bacillus (Gay, 56). The clinical use of such a serum is still in the experimental stage.

In Egypt, where both types of bacillary dysentery occur in very severe form, serum treatment has been successfully employed. A series of 84 cases were treated with a multivalent serum and there were seven deaths. The mortality in the same hospital in cases treated without serum had been about 60 per cent. (Ruffer and Willmore, 125).

g. Antityphoid Serum

Attempts to treat typhoid fever with immune sera have met with but little success. The serum of Chantemesse (33) is obtained from horses immunized for a year or more against typhoid bacilli and against toxins obtained from old broth cultures. According to the reports of Chantemesse, the serum shows both opsonic and antitoxic properties when tested in laboratory animals. In his clinic, patients are given an injection of about five drops subcutaneously, and the temperature usually falls within ten days after the injection. Enlargement of the spleen, an increase in the blood pressure, a rise in the opsonic index, and improvement in the general appearance of the patient have also been noted.

From 1901 to 1907 one thousand cases were treated with a mortality of 4.3 per cent. The mortality for typhoid fever in other Paris hospitals during the same period was 17 per cent. Except by Chantemesse, the serum has not been extensively used.

Others have tried to neutralize the typhoid endotoxins by injecting sera of animals immunized against extracts of the bacilli (Kraus, 87; Hewlett and Goodall, 67). The patients appear to be better after the injections, but the mortality percentage has not been distinctly affected.

h Anti-Colon-Bacillus Serum

Various experimenters have attempted to produce a curative serum for use in colon infections, but with very little success. To be of any value the serum must be obtained by immunizing an animal against a great number of different strains. The most favorable results have been reported in local applications in cystitis and pyelitis, but may be due largely to the action of the substances normally present in any serum (see p. 172).

i. Antistaphylococcus Serum

There are several antistaphylococcus sera on the market, but very little is known experimentally or clinically as to their value. The staphylococci produce a soluble hemolysin, a leukocidin, and possibly other

toxic bodies in culture. Substances which neutralize these can be produced in immune serum, also agglutinins and bacteriotropins, but apparently such antibodies have little or no curative effect. In staphylococcus infection, better clinical results are obtained with vaccines than with immune serum.

j. Antianthrax Serum

The serum of animals immunized to anthrax has been used with considerable success in veterinary medicine. It is apparently just as valuable in human infections, although it has not been extensively tried. The best results seem to follow large intravenous injections up to 150 c. c.

k. Anticholera Serum

Specific bacteriolytic sera have a distinct protective influence on experimental cholera infections; but they have but little effect on the intestinal infections in man. Kraus produced an antitoxic serum by immunizing animals against the El Tor vibrio, a closely related species which produces a soluble toxin. This serum is apparently harmless and possibly of some value, judging from the mortality statistics, especially if used early in the disease.

The sera of animals immunized to bacterial extracts have given good experimental results, but there are no clinical reports as to their value.

l. Antiplague Serum

The best known serum is that of Yersin, which is prepared by inoculating horses intravenously, first with killed, and then with living, cultures of plague bacilli (Dujardin-Beaumetz, 41). This serum shows both antibacterial and antitoxic properties. Other sera have been produced by using the nucleoproteid or watery extracts of the bacilli as antigen. A serum containing antiaggressins has also been prepared by injecting animals with the peritoneal exudate of infected guinea-pigs.

The sera exercise a protective effect in man, which disappears in a few days after injection. Choksy (34) treated 1,203 cases with 49 per cent. mortality, and reported 74.5 per cent. mortality in cases treated without serum. Success seems to depend on intravenous injections of large amounts, 20 to 40 c. c., in the first few days of the disease. Masuyama (103) advocates large injections of serum combined with operative incision of the buboes as the best method of treatment.

III. Other Types of Immune Sera

a. Antituberculosis Serum

It is doubtful whether resistance to tuberculosis depends on substances in the blood, for it is not generally possible to obtain immunity by injection of serum from one animal into another. It has been found possible, however, to demonstrate numerous antibodies in the sera of immune animals (p. 149), and attempts have been made to treat the disease with such sera, although they have never been shown to have characteristic bactericidal or antitoxic properties. One of the earliest attempts at the production of a therapeutic serum was made in this country by de Schweinitz, but its use has been abandoned.

Marmorek's antituberculosis serum is the best known (102). This is obtained by injecting horses with young bacilli cultivated on a special medium. These bacteria are very slightly acid-fast and supposably more easily absorbed than ordinary bacilli. The animals are subsequently immunized to streptococci from phthisical sputum, so that the serum is both antituberculous and antistreptococcal. It is usually injected subcutaneously in doses of 5 to 10 c. c., given daily for eight days, then omitted for eight days, and the course repeated. This treatment not infrequently gives rise to severe reactions, which are attributed either to toxins set free by bacteriolytic action or to serum disease. It has been given intravenously and per rectum, and also injected directly into cold abscesses. It has been extensively tried in many clinics. Stephani reports its use in fifty-eight cases which had not improved under climatic or other forms of treatment, 67 per cent. of which were benefited. It is hard to reconcile such favorable reports with those of others who have decided, after thorough trial, that it is of little or no value.

Maragliano's serum is prepared by the injection of horses, cows, or calves with filtered cultures of virulent young tubercle bacilli, and also with extracts and emulsions of dead organisms. He claims to have demonstrated both antitoxic and bacteriolytic properties in this serum, but others have failed to confirm his results (101). He advises its use in incipient cases, and good results have been reported from some Italian clinics. This preparation has been used little outside Italy, but experience with it at the Phipps Institute in Philadelphia indicated that it was of very little value.

Vallée (144) has prepared a serum by injecting horses, first with attenuated, and then with virulent, living bacilli. The serum is not bactericidal, but animals immunized with it acquire the power of confining tubercle bacilli to the point of injection and resisting a general infection. The value of this serum has not yet been tested in man.

Ruppel and Rickmann (126) have recently produced a serum which is prepared in horses by first sensitizing the animals to tuberculin by injecting living tubercle bacilli intravenously, and then immunizing them by increasing doses of tuberculin. Most of the antibodies found in antituberculous sera may be demonstrated in this preparation, and it also has the power of rendering tuberculin atoxic when mixed with it in vitro, and has a certain protective action on laboratory animals.

This preparation was tried in twenty cases of severe tuberculosis, a few of which showed very striking improvement, and has also been used in combination with tuberculin.

Spengler (138) has introduced a preparation of tuberculosis immune bodies called I. K. on the theory that these are contained in the red corpuscles. The antibodies are freed from hemoglobin and albumin, but he does not state the method of preparation. Most of those who have attempted treatment with I. K. agree that it is worthless.

b. *Antithyroid Serum*

On the theory that the symptoms of Graves' disease are produced by intoxication with excessive thyroid secretion, an antithyroid serum has been prepared by Beebe and Rogers (8) for the treatment of this condition. By injecting rabbits with the proteins of human thyroids, they obtained a serum which they consider has specific cytotoxic properties against human thyroid cells. Others have doubted the existence of cytotoxins specific for any organ, but in any case precipitins can be demonstrated in this serum; and, when injected into other rabbits, it neutralizes, to a certain extent, the toxic effect of human thyroid protein. In patients with the symptoms of severe thyroidism the serum often relieves them in a manner suggesting true antitoxic action. Only certain individuals respond to this treatment. The serum acts most favorably in early cases of typical exophthalmic goiter. In atypical cases, where the symptoms point to an abnormal rather than an excessive thyroid secretion, some benefit has followed combined treatment with antithyroid serum and sheep thyroid (see also Vol. III, Sec. IV, Chapter VII).

c. *Deutschmann's Serum*

This is a non-specific serum obtained from animals which have been fed with large quantities of yeast. There is also a Serum E which consists of the globulins of the original serum precipitated by distilled water. It is supposed to be useful in all forms of sepsis, and to act on the leukocytes as a stimulin; and perhaps also to stimulate the formation of antibodies. However, tests for various antibodies in vitro and for protective

action in laboratory animals have shown very little difference between Deutschmann's preparation and normal serum (Bockhoff, 18).

Good results are reported from Deutschmann's clinic in septic infections of the eye, but in the hands of others the serum has given negative results. Deutschmann advocates daily subcutaneous injections of from 4 to 8 c. c.

d. *Autoserotherapy*

Favorable results have from time to time been reported in cases of tuberculous pleurisy with effusion, from the injection of small amounts (1 to 5 c. c.) of the exudate into the patient's subcutaneous tissues. This method was first introduced by Gilbert (57); and results in many instances in a prompt absorption of the exudate after from one to six injections (Schnütgen, 129). It seems to have no effect in mechanical hydrothorax and very little on exudates of other than tuberculous origin. The method is purely empirical; some assume the presence of tuberculin in the fluid; others, on quite as insufficient grounds, the presence of bactericidal and antitoxic substances. The injections are usually followed by a febrile reaction which may be a factor in the results.

e. *Human Immune Serum*

Various attempts have been made to produce immunity in patients by injections of serum from individuals who have spontaneously recovered from the same disease, especially in conditions where it is not easy to produce a similar immunity artificially in animals. Unfortunately, in the blood of those who recover from a natural infection antibodies are never present in a concentration comparable to that produced by artificial immunization, and the transfer of small amounts of such weak serum is ineffective. The method has been tried in typhoid fever, epidemic meningitis, pneumonia, infantile paralysis, and streptococcus septicemia, but without satisfactory results.

Serum Therapy in Spotted Fever

The serum of horses which have recovered from injections of the virus of Rocky Mountain spotted fever contains substances which protect guinea-pigs from infection. By repeating the injection and then precipitating the globulins from the serum a fairly powerful preparation was obtained by Heinemann and Moore (65a). There are as yet no reports on its therapeutic use.

F. PASSIVE NATURAL IMMUNITY

It is possible that natural as well as acquired immunity may be in part transferable from one individual to another, and normal serum and extracts of normal cells have from time to time been used therapeutically in the effort to produce a passive natural immunity.

I. Normal Serum

Various antibodies are present in normal serum, and many pathological conditions are attributed wholly, or in part, to a deficiency of these or of other normal constituents in the patient's blood. In a number of widely varying conditions attempts have been made to overcome this hypothetical deficiency by injections of normal serum. These injections appear to control the hemorrhage in many cases of hemophilia and purpura, and some clinicians have reported success in the treatment of eclampsia, toxemias, and septicemias. Recently normal serum has also been applied locally in surgical conditions where the serum of the blood stream does not have free access to the lesion.

Antiferment Treatment.—The use of normal serum locally in suppurative processes is referred to as "antiferment treatment" (McEwan, 99). The solution of tissue about acute abscesses is due to the digestive action of a leukoprotease set free by the disintegrated leukocytes, and the intoxication produced by such infections is supposed to be due to absorption of the products of this digestion. Normal serum contains substances which inhibit this process, probably the same body as antitrypsin. It is a thermolabile substance present in larger quantities in human than in most animal sera, but may be increased in animals by immunization with trypsin. According to this method abscesses are opened by puncture instead of incision, the cavity being washed with salt solution and then filled with the serum. Open wounds are packed with gauze saturated with serum. The serum may be obtained from the patient or from a normal individual by puncturing a vein; or sterile ascitic fluid, fresh or concentrated *in vacuo,* may be used. Normal animal serum contains less antitrypsin, but the serum of animals immunized to trypsin is now sold under the name Leukofermantin; and animal serum concentrated *in vacuo* at a temperature of 20° to 30° C. is also recommended. If there is any doubt as to the sterility of the serum, it should be filtered through a Berkefeld or porcelain filter. Good results in well localized infections have been reported from many clinics, the injection promptly relieving the pain in the abscess and the toxic symptoms. The treatment has usually failed in phlegmonous or diffuse processes.

The antiferment treatment has also been applied to malignant tumors

by injection of normal serum, together with cholesterin, quinin, and other substances which inhibit ferments, in the neighborhood of the tumor, or directly into the tumor mass. The results have not been encouraging (Hofbauer, 70).

Fresh serum is bactericidal to many strains of colon bacillus, and has been instilled into the bladder as a cure for cholecystitis. It has also been used subcutaneously in the treatment of puerperal septicemia (Welch, 156).

Serum Treatment of the Toxemias of Pregnancy.—Eclampsia and the psychoses and dermatoses of pregnancy are usually attributed to toxemia, and the use of horse serum has been advocated on the theory that the intoxication is produced by a ferment or toxin from the placenta, against which there are antibodies in normal serum (Freund, 52). After the patient has been bled, 20 to 80 c. c. of the serum are injected intravenously. Success has been reported in the small number of cases treated. Others prefer to use the serum of normal pregnant women in which they think the antibodies must be more abundant (Mayer, 104). Normal human serum has also been used with apparent success in these conditions, as well as in the treatment of other forms of urticaria, and of various infantile dermatoses (Linser, 94).

Serum Treatment of Hemorrhagic Conditions.—Serum has also been used to control hemorrhage (Weil, 155), and success has been reported in hemophilia, purpura hæmorrhagica, and hemorrhage from other causes treated by subcutaneous injections. Rabbit serum or horse serum is most frequently used, in doses of 10 to 40 c. c., frequently repeated (Leary, 91). Some prefer normal human serum (Welch, 156). The results seem to be better when the serum is quite fresh. Perhaps the simplest method is to draw 20 c. c. of blood from a healthy donor by means of a sterile glass syringe, and inject this directly into the patient, either subcutaneously or intermuscularly, before the blood coagulates. Whole blood injected in this way is rapidly absorbed.

While the mechanism of its influence is not understood, the value of the treatment seems to be empirically established. Experience is as yet too limited to determine in just what class of hemorrhagic conditions good results may be expected, but, from a considerable series of cases at the Sloane Maternity Hospital, it would seem especially valuable in hemophilia of the new born.

Intramuscular injections of 10 to 50 c. c. of fresh defibrinated human blood have been used in the primary pernicious and severe secondary anemias. The benefit in such cases is thought to be due to stimulation of blood formation, and not to a direct transfer of erythrocytes (Huber, 73). Direct transfusion has also been tried, and, while often of value in secondary anemia due to hemorrhage, has often proved dangerous or even rapidly fatal in the progressive pernicious anemias of the Biermer type.

Preliminary tests should always be made *in vitro* for hemolysins, agglutinins, or hemopsonins with blood from donor and recipient (Hopkins, 71). Serum obtained from the renal vein of goats has been used in nephritis, a procedure which seems somewhat fantastic (Spellman and Parisot, 137).

Normal Serum in Alimentation.—Injections of human serum have also been used as a means of alimentation, especially in marasmic infants. The use of horse serum, heated to 62° C. for half an hour to prevent serum sickness, has also been advocated for a similar purpose (Kirton); others use human ascitic fluid (Carter, 32). To obtain good results, it is necessary to inject large amounts, 30 to 150 c. c.

II. Leukocyte Extract

The usual method by which an organism rids itself of invading bacteria is through intracellular digestion in the leukocytes. It has also been thought by Metchnikoff and others that the cytase produced by destruction of the leukocytes is an important factor in the extracellular destruction of bacteria. Hiss and Zinsser (68) have prepared an extract by injecting rabbits intrapleurally with aleuronat suspensions, washing the leukocytes in the exudate so obtained, and digesting them with distilled water. They have used this extract in the treatment of numerous infections, principally those in which the bacteria act through their endotoxins, and in which immune sera have proved to be of little value. They have been able to protect animals against experimental infections with numerous organisms by injections of this extract, and they have obtained encouraging results in the treatment of lobar pneumonia, epidemic meningitis, and staphylococcus infections in man, and apparently distinct success in the treatment of erysipelas.

G. TREATMENT WITH BACTERIAL PRODUCTS

The use of lactic acid bacilli to inhibit intestinal putrefaction is familiar to all, and recently cultures of staphylococcus aureus have been recommended to remove diphtheria bacilli from the tonsils of bacillus carriers. The enzymes and toxins of bacteria have also occasionally been used, not to produce immunity, but on account of their directly destructive action on parasites or diseased tissues. Two of these preparations have aroused so much discussion that they deserve mention.

I. Pyocyanase

The B. pyocyaneus produces a proteolytic enzyme in culture which has a destructive action on other bacteria (anthrax, typhoid, diphtheria).

Emmerich and Löw (44) have prepared this nuclease for therapeutic use, especially in diphtheria. Applied locally, it has a marked effect on the diphtheritic membrane, but does not neutralize the diphtheria toxin (Strubell). While it seems hardly justifiable to substitute this for the antitoxin treatment, it has proved of some value in removing the bacilli from the throat in cases where they persisted after convalescence. Sörenson (130), after trying it in comparison with other disinfectants, found that it was successful in some cases where nitrate of silver had failed, but was slightly inferior to Loeffler's menthol-toluol-iron solution. It has been used locally in treating anthrax. The substance is prepared by filtering broth cultures of B. pyocyaneus which have grown for several weeks, through a Berkefeld filter, concentrating *in vacuo,* and dialyzing against running water. The ferment is then precipitated by alcohol and preserved in dried form.

II. Streptococcus and Prodigiosus Toxins in the Treatment of Tumors

An attack of erysipelas has, in a few instances, been reported as causing the regression or even disappearance of sarcomata; and Fehleisen (46) claimed to have cured cases of carcinoma by inducing erysipelas by inoculations of streptococcus cultures. Coley (37) and others, influenced by these statements, have attempted to treat malignant tumors by the injection of killed cultures and filtrates of cultures; and the preparation now recommended by Coley is a bouillon culture of streptococcus sterilized by heat, to which a certain amount of a sterilized agar culture of B. prodigiosus has been added. Increasing doses are injected subcutaneously, or later directly into the tumor. It is probable that the toxins have a harmful effect on the sarcoma cells, as the tumor occasionally breaks down; but it is not unlikely that the inflammatory reaction about the tumor has much to do with the outcome. The effects of the injections are very severe, and in some instances the death of the patient has undoubtedly been hastened. Coley recommends the use of the fluid in all cases of inoperable sarcoma; and, in certain cases of the relatively benign sarcoma of the long bones, as preferable to amputation. He also recommends it after the operative removal of sarcomata, to prevent recurrences. It is acknowledged to be of no value in carcinoma, but Coley reports a number of cures of sarcomata by this treatment, though chiefly of the more benign varieties, and Loeb (95) collected 78 cases with 5 per cent. of cures, which is certainly a high proportion; but no statement is made as to whether a microscopical examination was made of the tumors or not. On the other hand, many surgeons have been unable to obtain the slightest success with this method of treatment, and it should never be used where operative interference offers the slightest hope.

H. IMMUNE THERAPY AND MALIGNANT DISEASE

Spontaneous cure of carcinomata or sarcomata has been observed with extreme rarity in man, while in animals it is not infrequent. This phenomenon has led to an enormous amount of investigation of the conditions under which such cures occur in animals, without as yet any satisfactory explanation, much less any practical application, having been obtained. It has, however, been shown that a certain proportion of mice and a few other animals can be immunized to tumor implantations under strictly limited conditions. Again it has been found possible in suitable animals to cause actively growing tumors to regress or disappear by the injection of emulsions of the tumor; or even of normal blood or tissues other than their own. A slight but inconstant immunity has even been noted by Woglom (158) following injection of the animal's own spleen. The immunity obtained by any of these methods, however, is a tissue phenomenon, and can not be transmitted by the mere injection of serum or even by the transfusion of the entire blood mass of the immune animal, unless the recipient already has a growing tumor. The immunity does not, therefore, correspond with that observed in infectious diseases (Beebe, 7). The favorable results obtained by Hodenpyl (69) in carcinoma cases from the injection of ascitic fluid derived from an arrested case of general carcinosis were, in all probability, due to the stimulating action of the serum administered, and not to any immune body in the fluid. This is shown by the fact that quite as good effects have been obtained by the injection of fresh human serum from the placenta. The serum of animals immunized against human carcinoma tissue has also been used. Such sera contain numerous antibodies, such as precipitins and cytoxins for albumin and cells of human origin, but possess no specific action against tumor cells. A variety of attempts have also been made to treat malignant disease in human beings with injections of a great variety of tumor cell emulsions (Coca and Gilman, 35), and more or less modified extracts of tumor cells (Vaughn, 145), with a few suggestive results. Even autolysates of human fetal tissues have been tried (Fichera, 47), with the idea that, as children rarely have carcinoma, there must be some antisubstance in fetal tissues.

On the whole, however, neither active nor passive immunization has as yet proved to be of any definite clinical value, even though temporary regression of the tumor has occasionally been observed. The possibility of a spontaneous cure must always be held in mind in judging of the results in any individual case, and many of the results obtained are doubtless due more to the stimulation of the normal tissue resistance to the extension of the growth than to any direct action on the tumor cells themselves.

I. METHODS OF ADMINISTRATION OF SERA AND VACCINES

The usual method of administering sera or vaccines in man is by subcutaneous injections. The slow absorption from the areolar tissue is usually advantageous in the case of vaccines, but may interfere with the efficacy of antitoxin. Madsen injected subcutaneously 20 c. c. of anti-diphtheritic serum (9,000 units) into a healthy man. Five hours after the injection his serum contained only 0.1 unit of antitoxin, the amount increasing to a maximum of 1.13 units only after three days. Two weeks after the injection the serum still contained 0.14 unit per c. c. Absorption from the muscles is five to seven times as rapid as from the subcutaneous tissues, and injections may be made deep into the glutei or the muscles of the thigh. If immediate action is desired, recourse may be had to intravenous injections. These need never be used in active immunization, but in severe cases of diphtheria, for instance, or in cases where tetanus has already developed and the outcome of the treatment depends entirely upon the promptness with which the serum reaches the toxins, intravenous injections are of the greatest value. Administration by mouth cannot be recommended, as both antibodies and antigens are destroyed by peptic and in time by tryptic digestion; and absorption from the alimentary tract is very uncertain. Serum is absorbed to some extent from the rectum, but the favorable results reported after oral or rectal administration are probably largely due to accidental improvement in the patient's symptoms coincident with the exhibition of the remedy. Neither of these methods should be used if good results are expected.

In local infections it is often of advantage to bring the immune bodies into direct contact with the invading organisms. In meningitis the serum is introduced subdurally; and in tetanus injections into the tissues about the wound are used.

Injections may be made with any syringe which can be sterilized by boiling in one per cent. sodium carbonate. The all-glass syringes are the most convenient from many points of view. They are easy to clean, with strong acids if necessary, and the condition of the fluid to be injected can be easily observed. This is important, as small particles of cork or other foreign matter accidentally present in the fluid will give rise to serious irritation if introduced into the tissues. The only drawback is that the all-glass syringes are more fragile than those made with asbestos packing and metal tips. The needle should be large enough (No. 20) to allow the serum to flow through without great pressure. Platinum needles are very convenient, as they can be cleaned and sterilized by heating in a flame, but they are very expensive, and in the smaller sizes difficult to keep sharp. With children or delirious patients who are likely to move about, it is advisable to connect the needle to the syringe with a

short piece of rubber tubing. The needle and syringe should be sterilized by *boiling* for at least five minutes in 1 per cent. sodium carbonate solution. The plunger and needle of the glass syringe should be removed before boiling, and an asbestos-packed syringe should be partly filled with the solution. It is, of course, essential not to touch the shaft of the needle with the hands after it has been sterilized.

Very small subcutaneous injections (2 c. c. or less) may be given in the arm near the deltoid insertion. Larger injections may be given in the interscapular region, or, if the patient is in bed, in the anterior abdominal wall. When the amount to be given is over 10 c. c., it is well to divide the dose and give several injections in neighboring areas, as the procedure is then less painful. Intramuscular injections may be made into the quadriceps extensor femoris, the lumbar muscles, of the glutei. Intravenous injections are best made into one of the cubital veins. A rubber tourniquet or bandage is placed about the upper arm tight enough to constrict the veins and cause them to distend. The needle is introduced through the skin directly into the distended vein, and, when the vein is successfully entered, as shown by blood dripping from the free end, the syringe is attached, the tourniquet is loosened, and the serum is very slowly injected. It is safest to inject drop by drop. One should make sure that the syringe contains no air bubbles, and the serum should be warmed approximately to body temperature before the syringe is filled. Sera which contain antiseptics should not be given intravenously in very large amounts, but as much as 18 c. c. of a preparation containing ½ per cent. phenol has been given without producing any urinary changes. In animals, and probably in man, the danger of severe reaction is much greater after intravenous injections; in patients who have previously received serum treatment, it may be well to precede the injection by a small vaccinating dose. The technique of subdural injections is the same as that for lumbar puncture (see Vol. II, Sec. I, Chapter XII). The patient lies on his side with the knees drawn up as far as possible, so as to separate the spines of the vertebræ. The skin over the lower portion of the spinal column is cleaned, and a long stout needle is introduced between the third and fourth lumbar spines, this space being at the level of the iliac crest. The needle is inserted forward and slightly upward through the interspinous ligament to a depth of about an inch and a half in the spinal canal. When the needle reaches the subdural space fluid will drip freely from the end. After 20 to 30 c. c. of spinal fluid have been withdrawn, the syringe is connected with the puncture needle by a short rubber tube, and an amount of serum equal to the quantity of fluid removed is very slowly injected. The serum should be warmed to about body temperature.

J. CONCLUSIONS

Efforts to apply the principles of immunity to prophylaxis and therapy have met with greatly varying degrees of success in different diseases. Smallpox has been almost eradicated from civilized countries by the use of vaccine. In diphtheria, antitoxin confers an equally high degree of immunity, though of very short duration. The value of antityphoid vaccination is also fairly well established, although the protection conferred is by no means so absolute nor so long-standing as that in smallpox. Inoculation against plague seems to be useful, and it is possible that similar methods may finally prove important against cholera and dysentery. Rabies and tetanus can be almost certainly prevented if immunization is begun early in the incubation period. So much is certain in the prophylaxis of infectious diseases.

In the treatment of the disease, after the symptoms have developed, antidiphtheritic serum and, to a less extent, antimeningitis serum are of established value. Antitoxin is also apparently helpful in the treatment of tetanus after the outbreak of symptoms, and antivenin and antistreptococcus serum have given encouraging though far from satisfying results. The value of bacterial vaccines in certain chronic staphylococcus and gonococcus infections seems established, and there is reason to hope that some success may follow their use in other chronic infections, and even in pneumonia and typhoid fever. In experienced hands tuberculin is certainly beneficial in selected cases, but too little is yet known of its action to warrant the general use of this most powerful drug by the practitioner.

The attitude of the general practitioner toward these various therapeutic measures must depend largely on the statistical results, and not on theoretical considerations. Of the many preparations described, there are five on which the physician can rely. There is, for example, no drug in the pharmacopeia the value of which is better established than is that of diphtheria antitoxin, and the invariable use of serum therapy in diphtheria and also in cerebrospinal meningitis is clearly indicated in the light of our present knowledge. The duty of the physician to vaccinate his patients against smallpox and to immunize those in whom infection with rabies or tetanus is suspected also seems plain. In such desperate conditions as developed tetanus and streptococcus septicemia the use of serum also seems justified, even though its value is much less certain. There are a number of other specific preparations which the practitioner may occasionally find useful, but, in regard to most of them, it should be remembered that their application is still in the experimental stage; and that the greatest caution is necessary to avoid occasional injury to patients by their administration. The place for the trying out of such methods is the hospital or clinic, where results can be more thoroughly

observed and controlled than in private practice, and statistics of large series of cases collected. The greater part of these preparations, especially the tuberculins and other vaccines, are potent for harm in inexperienced hands, and it would probably be better for the community if they were used only by those whose laboratory training and wide experience enable them to make a special study of such forms of treatment. Even in clinics, trial should be confined to methods the efficacy of which has been tested in the laboratory. The very valuable work of Wright and his pupils especially has led to an unfortunate tendency to the indiscriminate and aimless use of vaccines, even in the treatment of conditions which have never been shown to be of bacterial origin. Little but harm can result from such random experimentation. Immunization against diphtheria and vaccination against smallpox were not attempted clinically until the probability of success had been clearly indicated by experiments on animals in the one case, and by study of spontaneous human infections in the other. Not all the methods of immunization that have given promise of success when tried in the laboratory have proved useful in the clinic, but, on the other hand, good results have never followed the introduction into practice of methods of immunization which were not based either on laboratory experimentation or on carefully developed theories supported by clinical observation. However, it is not to be doubted that, by the cautious and systematic application of new laboratory methods to the treatment of infections in man, other forms of immune therapy will be discovered of as great importance as the serum treatment of diphtheria or vaccination against smallpox.

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CHAPTER IV

HYDROTHERAPY AND BALNEOLOGY

William J. M. A. Maloney

HYDROTHERAPY

Historical Introduction

Man from his advent has daily experienced the beneficent action of water. Instinctively he drank when thirsty, washed when unclean, and bathed when tired and heated. The knowledge that water is essential to the maintenance of life was among the first of all human acquirements. The relation of vegetation to water and the cleansing action of the rain, streams, and seas must have been recognized even by the earliest forms of human intelligence. Primitive man felt the need of water, saw its wide dominion in the world, wondered, perhaps, at the mysterious forces which dictate its form and motion: and in his dawning imagination endowed it with preternatural powers.

Symbolism characterizes all primitive mental expression. It was therefore natural that man should use water, not merely when ministering to his bodily cleanliness, but also when striving to convey ideas of moral purification. As late as the beginning of the Christian era we find this application of water even among the cultured Romans. Pontius Pilate, when he wished to disclaim all guilt and responsibility for the Crucifixion, called for water and washed his hands before the comprehending eyes of the clamoring mob.

Analogous use of water entered into spiritual matters. To-day Hindoos still seek grace by bathing in their sacred streams; Mohammedans perform extensive ablutions as an essential preliminary to prayer; Jews wash in prescribed fashion at fixed periods in order to conform to the law; and Christians are sprinkled with, or immersed in, water to wash them from the stain of "original sin" in the sacrament of baptism.

This symbolic use naturally led to the inclusion among religious practices of the application of water in the treatment of mere bodily ailments. So hydrotherapy developed under sacred auspices, and the use of water as

a healing agent acquired the dignity of a religious ceremony. Waters from sources distributed over the greater part of the Old World gained more or less local reputations for special efficacy. Sometimes a natural peculiarity lent awe to these waters and served to strengthen faith in their remedial powers. The periodic filling of the well of Bethesda in Jerusalem and the annual rise of the Nile are typical examples of such peculiarities. The moment of the appearance of these unique phenomena signified to the faithful that the endowed waters had then attained the climax of their curative powers.

In some instances the special attributes of the waters were disclosed by revelation or by happy experience to the pious. To some sources was given a specific virtue; thus, the famous well of St. Triduana and the waters of Siloam were efficacious in eye diseases; lepers were made clean in the Jordan; abdominal diseases were healed at the well of St. Gingolph; and madness, sterility, and most other afflictions were cured by waters from appropriate sources. The Jordan, the Nile, the Ganges, the well at Emmaus, and a few other holy waters possessed so wondrous powers that they acted practically as panaceas.

The waters of Bethesda now rise almost unheeded; the pious blind no longer seek the once all-powerful well of St. Triduana; and, except among the adherents of the Greek Church, faith in the properties of the sacred waters of the Jordan is almost dead. As the popularity of one source ebbed that of another rose. In our own times to the well at the Grotto of Lourdes, near the Pyrenees, and that of St. Winifred at Holywell, in Wales, seem to have been transferred many of the marvelous properties which centuries ago were vested in the holy places of the Orient. From these wells wonderful cures are daily reported by eminent physicians whose belief in the verity of the phenomena they record is above suspicion and beyond question.

[The *modus operandi* of these cures may be just as satisfactorily explained in other ways and, moreover, the cures can be performed in many other ways.—Editor.]

Although substances of greater potency, but of less traditional and spiritual force, have had their day and now are irretrievably forgotten, water has preserved throughout the ages its reputation as a remedial agent, owing largely to this fostering by religious bodies of faith in hydrotherapy.

The rudely material benefits of bathing were early appreciated. So widespread in ancient times was the custom of bathing that the Greeks and Lacedæmonians had not only private, but public baths. Alexander the Great is recorded to have marveled at the magnificence of the baths of the conquered Darius. But *the* apostles of bathing were the Romans. The Romans elevated bathing to a cult. The splendor of their baths is a salient feature of their civilization. In the Roman conquests a bath was

built as soon as the barbarians gave the invaders a moment's leisure. The more settled the new colony the more ornate was the bath. Elaborate descriptions of these early baths and interminable dissertations upon bathing survive in the writings of many of the ancient authors, particularly Pliny, Seneca, and Juvenal. The use of water alone was not fashionable even in the humblest baths. Oils, perfumes, spices, and other adjuvants enhanced the esthetic pleasures of these institutions. Together with bathing the Romans associated massage and physical exercises. The untrammeled license which characterized many of the public baths of the Romans brought bathing under the ban of the reforming zeal of the early Christian Fathers and perhaps conduced to the not over-scrupulous cleanliness which sometimes served to eke out the penance of the pious anchorites who retired into desert places, and to the strikingly insignificant rôle which water plays in the ritualistic practices of the Christian church.

The Roman influence upon bathing is accentuated in our period partly because the Romans were so prodigal in their bathing resources, but mainly because our civilization is in direct succession to theirs. But knowledge of the cardinal uses of water probably dates from the dawn of man. The ancient Egyptians, Picts, Celts, Turks, Moroccans, Japs, Indians, and Mexicans all used forms of vapor baths. Besides baths of water—ice, vapor, hot, cold, river, spring, well, and sea water—other media such as sand, mud, peat, wine, milk, and even blood were used.

The therapeutic use of water by physicians is as old as the art of medicine. Hippocrates was hardly an enthusiast for baths, but he advocated them under certain conditions in several of his writings. Celsus praised house baths but was reticent about the use of mineral waters. Aretæus of Cappadocia, Athenæus, and Rufus of Ephesus wrote at length upon the merits of certain thermal baths. Agathinus was the apostle of cold baths. Galen said little of baths. Fallopius alluded to the diseases which may be benefited by the water at Lesbos, Mitylene, and other places. Antyllus, Oribasius, Ætius, Paul of Ægina, Cælius Aurelianus, and countless others through the ages lauded the uses of water. To enumerate the physicians who have practiced water treatment would be merely to catalog the fathers of medicine. But until the scientific renaissance of the last century the properties and actions of water remained clouded in superstition and empiricism. The pioneer work of Winternitz, Brutenbach, Baruch, Thayer, and others has now definitely established the physiological principles upon which the action of water depends. Out of the chaos a certain amount of order and system has been evolved; a rational basis for the therapeutic employment of water has been defined; and the science of hydrotherapy, which deals with the action of water upon the human body, has been erected.

Here we shall confine our attention almost exclusively to water. The physical characters of water will first be considered; then the physiologi-

cal principles of its various actions will be discussed; next, the ways in which it can be used will be described; and, finally, its application to disease will be dealt with.

Properties of Water

A brief outline of the properties of water is essential to a clear understanding of its uses. Its distribution is universal. It exists in and can readily be transformed into solid, liquid, or gaseous form. Under ordinary atmospheric pressure, at the temperature of 0°C. it becomes ice; between 0° and 100°C. it is liquid; about 100°C. it exists as steam. In changing from fluid to ice a remarkable absorption of heat takes place: if a kilogram of water at 0°C. and a kilogram of water at 79°C. be mixed the resulting mixture has a temperature of 39.5°C.; but if a kilogram of ice at 0°C. be added to a kilogram of water at 79°C., the ice disappears and two kilos of water with a temperature of 0°C. remain. This heat absorption explains the great efficacy of ice baths in bringing about a lowering of temperature in cases of fever. Similarly in passing from liquid to steam a tremendous amount of heat is rendered latent; hence allowing water to evaporate from a surface is one of the best means to produce cooling. Further, water has a great capacity for absorbing heat; thirty-one times as much heat is required to raise one unit of water through one degree of temperature as is required to raise one unit of platinum one degree. Water cools relatively slowly. It is therefore invaluable as a medium for abstracting heat, for storing heat, and for applying heat. Its utility as a thermal agent is further enhanced by the ease with which its temperature can be measured, regulated, and controlled. As a fluid it mixes with solids to form pastes, the consistency of which can be altered at will; it also permeates most textures, so that its application can be restricted or adapted at will to any surface. It is the most universal of all solvents: its solutions of salts and gases are applied externally as baths; it is an ideal vehicle for the administration of all soluble substances, and it is used in the economy as a distributing and eliminating medium.

Water can readily be applied with varying and regulated pressure. This property is utilized in forms of spray and douche baths.

When water holds a small amount of a salt in solution it is one of the best of the electrical conductors and can be used to insure intimate contact between the body and electrodes, or a bath may be arranged in a circuit, through which faradic or galvanic currents may be passed. When currents are passed through aqueous solutions decomposition or electrolysis of the solution occurs. Thus, the constant current decomposes water into hydrogen and oxygen. The elements at the moment of liberation from their compounds are said to be nascent. The action of the nascent ele-

ments produced by such electrolysis is relatively powerful and is utilized in certain forms of baths.

Water is thus an ideal medium for the application of physical agents owing to the simplicity, precision, and rapidity with which these physical forces can through it be controlled. Its power in combating disease depends almost solely on its property as a medium. Its physiological action is therefore essentially that of the physical force which it is conveying. We shall, therefore, before proceeding to the therapeutic uses of water briefly consider the actions of heat, cold, pressure, and electricity upon the body.

The pioneer work of Winternitz of Vienna laid the foundations of most of our knowledge of the physiological action of water. The chief sphere of hydriatic medication is the skin. The physiologic action of water upon the skin is very simple. So far as hydrotherapy is concerned the skin may be regarded as a great sheet of imperfectly sheltered blood vessels and nerves. The effect produced by water upon the skin is merely the expression of the reaction of the blood vessels and nerves to the physical forces applied by the water. Congestion or ischemia of a part depends upon the state of the blood flow in the capillaries; the capillary stream is controlled mainly by the contractibility or tone of the arterioles; and upon the condition of the arterioles hangs the efficiency of the whole circulatory mechanism. The skin is richly supplied with nerve terminals which are elaborated sometimes into special sensory end organs. Just as the network of vascular capillaries opens into larger channels and thus links the peripheral circulation directly with the heart, so the terminal cutaneous ramifications of the sympathetic and sensory nerves are gathered together into trunks and pass to the central nervous system. A stimulus to the skin thus may powerfully affect the vascular and nervous arrangements of the whole body. The skin is in fact an externalized regulating mechanism for the circulatory and nervous systems.

Some areas of the skin have certain definite nervous relations to the viscera. An organ may be reflexly influenced through a particular area of skin, and affections of organs may reflexly influence special skin areas. Our knowledge of these areas we owe to Head and Mackenzie, and it enables us so to guide and restrict our operations that by the simple bloodless procedures of hydrotherapy we can influence viscera with as much certainty as if we were exposing them by a surgical operation.

The skin, however, besides being an organ of sensibility, has also secretory, excretory, and heat-regulating functions. These are subservient to nervous and vascular control. A stimulation of a cutaneous secretory nerve induces an increased flow of sweat and a local increase in the blood supply. An increase in the blood supply usually involves an increased sweat secretion. The heat regulation of the body is largely attained through the skin. In overproduction of heat by excessive muscular action,

or in exposure to excessive external heat, the cutaneous capillaries dilate, and sweating increases; the evaporation of the sweat from the skin absorbs much of the surplus heat from the body. If exposed to cold the cutaneous vessels contract and sweating diminishes; the body heat is thus conserved. Urea, xanthin, and other decomposition products of proteid metabolism may be demonstrated in the sweat; the sweat glands, just like nearly all glands, have a vital selective affinity for certain substances circulating in their blood supply.

But as the secretory, heat-regulating, and excretory mechanisms are merely outward evidences of vascular and nervous activities we shall first consider the action upon these activities of each of the physical forces utilized in hydrotherapy.

Physical agents such as cold act mainly by virtue of their irritant properties. Within certain limits of intensity a stimulus to the skin produces similar effects, whether it be caused by chemical or physical action. Weak cutaneous irritants narrow the arterioles and raise the blood pressure; the increased peripheral resistance thus produced causes the heart to contract more rapidly. On the contrary, intense cutaneous irritants fatigue and paralyze the normally existing innervation of the blood vessels and produce a relaxation and dilatation of the peripheral arterioles with diminution of pressure; at the same time the inhibitory action of the pneumogastric slows and intensifies the cardiac contraction, and, when excessive, may produce death by vagus tetanus. (Roehrig and Naumann quoted by Baruch.)

Cold.—The application of cold is perceived with varying delicacy on different parts of the skin. The local and general disturbances are dependent upon the degree and duration of the cold employed and the extent of the area to which it is applied; i. e., to the intensity of the stimulus. Long-continued application of severe cold deleteriously affects the vitality of the tissues to a degree depending upon the resistance of the tissue exposed. And when the cold is severe, besides the coldness, a pain element is noticeable in the sensation.

The application of sudden cold produces first a sharp inspiration, next a pause, and then a long expiration which is followed by frequent and shallow breathing. This reaction is the basis of one of the best known and most efficient methods of resuscitation of the still-born; indeed, it is alleged to be an essential stimulus to the establishment of respiration at birth. In breech presentations, in which a premature onset of respiration might be attended by fatal consequences to the child, accoucheurs carefully swathe the extended limbs in warm clothes. The effect of cold is not confined to the respiratory mechanism; consciousness is stimulated by its application, as may be seen in the awakening of the dormant attention of hysterics, and in the sobering of the drunk, by cold affusions. Cold is one of the most powerful nerve stimulants we possess.

Owing to the stimulation of the cutaneous nerves the voluntary and involuntary muscles are influenced. Investigations by means of Mosso's ergograph have proved conclusively that cold is able to increase enormously the resistance of muscle to fatigue, and also to restore the efficiency for work to muscle which is already fatigued. A slight increase in the tonicity of voluntary muscle is produced. And in involuntary muscle the stimulation is evident in "goose skin," and in shivering.

This increase of muscle tone and of muscular action and the vascular redistribution which they cause serve to augment animal heat and partly to compensate for that which is being lost. Perceptible cold produces, partly by direct action and partly by reflex action upon the vasomotor center in the floor of the fourth ventricle, a local constriction of the blood vessels. The blood is, in consequence, diminished in the affected part, and a concomitant hyperemia is produced in adjacent areas.

The result of the contraction of the involuntary muscle fibers in the skin and of the sensory stimulus given to the central nervous system is a sudden diminution in the caliber of the cutaneous capillaries. This narrowing of the arterial and venous river bed raises the blood pressure, increases the endocardial stimulation, and causes an automatic increase in the force and speed of the ventricular contractions.

The increased cardiac action propels an augmented supply of blood through the capillaries, which are thus expanded to the fullness of their capacity. The increased force of the heart is maintained for some considerable time.

The contraction of the cutaneous vessels diminishes the skin secretion, increases the blood pressure in the vessels of the deeper structures, and stimulates their vital processes. One well-known consequence of this elevated blood pressure is diuresis. The increased blood pressure, the increased force and frequency of the heart's action and the increased blood supply to the kidney all tend to enhance the diuretic action of cold.

James Tyson measured the amount of urine and urea excreted daily by a patient suffering from enteric fever, who was being treated by cooling (Brand) baths. He found that the amount of urine secreted was vastly increased. Before the Brand bathing was begun the urine, as is usual in febrile conditions, was scanty and very concentrated. After the bathing, as much as 1,980 c. c. of urine were excreted daily. As the toxicity and the amount of contained solids were increased, not only was the mechanical transudation of fluid through the kidney augmented, but the selective secretory properties of the renal epithelium were enhanced also.

Experiments have proved that in addition to these changes there are also remarkable alterations in the relative proportions of the corpuscular elements of the blood.

Cold baths produce a leukocytosis which persists at least for one and a half hours. The increased blood pressure in the spleen and in the lym-

phatic glands, consequent on the general peripheral vascular contraction, may wash out the white cells from these viscera into the general circulation.

The reëstablishment of the normal ratio among the blood cells in the course of one or two hours from the time of the cold application shows the alteration in the blood to be due to transitory changes in the circulatory system, in the cardiac tone, and in the lumen of peripheral vessels.

Some observers have found an increase also of red cells.

On the other hand, brief application of cold to the general body surface results in an increased viscosity of the blood owing to the augmentation of the cellular elements.

If the application of cold be local, remote effects are still produced. These distant effects are of three classes: First, owing to the constriction of the blood vessels locally, the blood is driven into other areas. Thus Winternitz demonstrated that a cold hip bath augmented the volume of the arm. This may be termed the remote general action. Second, there is the symmetrical or intermediate response, that which affects one of a pair of structures affects the other: such is seen when, say, the right hand is immersed in iced water, the left becomes blanched and cold. So great is this action that Thomson states that a thermometer held in the left hand shows a fall of 2-5° F. under such circumstances, and he records a case where, during an operation upon a divided palmar arch, he produced vascular constriction in the injured hand by immersing the sound hand in iced water, and was thus enabled to proceed with his ligaturing unembarrassed by hemorrhage. Third, there arise reflex influences upon subjacent or remote viscera. In popular medicine this third category is well recognized. Girls sometimes foolishly immerse their feet in cold water to arrest imminent menstrual flow on the eve of some entertainment. Bleeding from the nose is treated by allowing a cold key to wander down the back. More precisely we now apply our treatment to Head's areas in order to insure the localization of the reflex action to the viscus which we desire to influence.

In order to obtain a cold stimulus what degree of cold must be employed? The body temperature in the axilla is 98.4°F.: but the average temperature of the whole cutaneous surface when clad with customary garments is probably about 92° F. (Winternitz). Hence to induce a "cold" reaction temperatures sensibly lower than 92° F. must be employed.

If the cold be slight, the effect does not proceed beyond the stage of arteriole constriction, enhanced cardiac and respiratory action, and increased muscle tone. And these consequences are in variable degree transient. The vasoconstriction is followed soon by vasodilatation; but the beneficial effect upon the heart and the general musculature is more persistent. While in the cold bath, when the cold is mild, or after emerging, if it be less mild, the cutaneous blood vessels dilate, the skin reddens, a

pleasurable sensation of warmth ensues, and a feeling of general well-being prevails. Such is the "reaction" to the cold bath. To elicit it in the sick great care is necessary to temper the stimulus to the patient's strength. The shock produced by the cold must not be too severe: and the reaction not too long delayed.

Heat.—As already stated, the initial effect of all forms of physical stimuli is essentially the same. Hence the action of heat is not directly inverse to that of cold. All stimuli produce initially vasoconstriction, but whereas with cold this effect tends to be maintained, with heat it is immediately superseded by vasodilatation which persists as long as the heat. Owing to the vascular dilatation the skin reddens, a sensation of warmth prevails, sweating increases, and the deeper structures are depleted somewhat of their blood. The increase of the cutaneous blood sheet promotes radiation, the evaporation of the excess of sweat renders latent a vast amount of heat, and the concomitant increased frequency of respiration abstracts much heat in the larger volume of expired air and water vapor: hence, all these factors tend to cause a fall of temperature. If the whole body be immersed in a bath of a temperature higher than 98.4° F. the body temperature may rise somewhat.

The relatively anemic condition induced in the viscera minimizes their activities and thus tends to act as a general sedative. Also, the direct action of heat upon the sensory nerves is pleasurable and soothing.

Under the influence of the hot bath it has been found that the viscosity of the blood is diminished; the blood becomes "thinner and more watery." This result is apparently brought about by an increase of the area of the circulatory system with consequent diminution of transudation of plasma into the lymph spaces, and increase in the watery elements of the blood tissue.

The result of hot and cold baths on respiration appears to be somewhat similar: in each there is at first a sharp inspiration; next, a pause, and then a long expiration which is followed by frequent and shallow breathing.

The chemical activity of the lungs is much enhanced by the hot bath, there being a huge increase of oxygen consumption and carbon dioxid excretion. Baruch attributed as much as 78 per cent. increase to the former, and 91 per cent. increase to the latter, after a bath of thirty minutes in which the body temperature was not greatly raised, and in which the number of respirations per minute was not increased.

On the other hand, hot baths diminish the power of muscular work, unless at the same time mechanical stimuli such as douches and massage are employed; but even with these adjuvants the increase in efficiency is always less than under the influence of cold applications.

Together with the increased muscular effort with which respiration is performed, increased production of carbon dioxid and increased absorp-

tion of oxygen occur also. This evidence of increased tissue respiration is due to the active katabolism which the tissues are undergoing in their effort to produce by combustion sufficient heat to compensate for that abstracted by the cold water. The effort is partly of reflex nervous origin (cf. the shivering) and partly consequent upon the flooding of the viscera by the blood which has been expelled from the constricted cutaneous circulation.

Roughly speaking, therefore, we may regard the action of cold as tonic, of heat as sedative.

Electricity.—Electricity produces upon the body effects which are physiological, electrolytic, cataphoric, and bactericidal. These effects will be discussed at length in the section upon electrotherapeutics.

Pressure.—The physiological effects of pressure will be discussed in the section on massage.

Mode of Application

The means employed to apply water are innumerable. Many elaborate apparatuses have been devised but, in proportion as their complexity increases, their usefulness as a rule decreases. Indeed, all the essential principles upon which hydrotherapy is based may be utilized through primitive domestic appliances. The ordinary full bath, partial baths such as hip baths, shower and douche baths, wrapping in wet sheets, and the application of compresses are the most important means by which water is applied. In all of these measures water is used essentially as a vehicle for the application of heat or cold. The temperature is either maintained as constant as is possible throughout the procedure, or it is designedly varied. Vapor and hot-air and radiant heat baths are conveniently studied here. These may also be full or partial.

The water baths may be medicated in various ways. Salt-water baths (one-third of a pound of salt to each gallon of water); alkaline baths (one-fifth ounce of sodium carbonate or one-tenth ounce potassium carbonate per gallon); acid baths (one-third ounce dilute nitrohydrochloric acid per gallon); mustard; bran; aromatic baths, such as lavender and pine; mercurial; ammoniated; sulphurated; and countless other varieties are employed.

The purpose of this medication is to add to the temperature effects, the bland or irritating, the sedative or stimulant action of the medicament.

Stimulant action is obtained not only by appropriate temperatures and medication, but also by suitable regulation of the duration of the application. At Nauheim stimulation is achieved by the impact of hosts of bubbles of carbonic acid gas upon the skin. Massage and friction bring about a similar but more powerful action. By projecting water at high

pressure against the body—douches, needle sprays—a similar result is obtained concomitant with the action of the water.

Hence, temperature, irritation or sedation and pressure, may all be readily applied by means of baths. The practitioner, to employ the remedial measure satisfactorily, must first clearly recognize the precise effects he wishes to attain; then consider what means are most simple, most practical, and most certain to procure these effects. There is nothing absolute in the facts herein set forth for the use of baths in various conditions. These facts are gleaned from standard authorities such as Winternitz, Baruch, Schott, and others. They are meant merely as guides to treatment. No one slavishly follows the pharmacopeial dose of drugs. Each patient is a new experiment. So the temperature, duration, composition, and frequency of the bath, and the use of pressure, or massage, must be as carefully considered and as judiciously altered as the dosage of drugs would be.

The bath may be general, or local, either applied to the entire body surface, or only to some part. The water may be brought into direct contact with the skin, or another medium, as a sheet, may be made the vehicle for its use.

General Baths.—*The Ablution.*—An oilcloth or rubber sheet, covered with a blanket, upon which is laid a sheet, is prepared on the bed of the patient. Each part of the body is consecutively exposed; a wet towel wrung out of water is laid on the uncovered area. With the flat of the hand rubbing is applied through the towel and then the towel is removed and the part dried. When the whole body is to be treated in this way it is best to take the parts in definite order. This is the method of Winternitz.

Baruch recommends for much weakened patients the following procedure: On the day following a warm cleansing bath the patient is wrapped in long-haired blankets, one passing around the body, under the arms, and inclosing separately the lower extremities; another enfolds the arms at the sides, and is tucked in about the neck and under the feet. Heat is thus accumulated at the surface. In ½ to 1 hour the face is washed with water at a temperature of 50° F. Next each part is in turn bathed, rubbed, dried by gentle friction, and re-covered.

When the patient has become accustomed to this the ablution may be given with the subject standing. He stands in 12 inches of water at 100° F., the attendant washing him down with his hands or with a towel, and pouring on parts of the body water at a temperature initially 80° F., but daily lessening till it reaches 60° F.

Patients unaccustomed to cold water may begin by a partial ablution involving only the face, neck, and chest, and gradually including the whole body.

Ablutions should always be rapidly performed. They are useful not merely as stimulants of the peripheral nerves and vessels, but also by the

reaction induced, as an index to the state of the patient. They are much employed as a preparation for other forms of hydrotherapeutic treatment.

The Half Bath.—There should be in the bathtub enough water to immerse the pelvis, and it should be at a temperature of 70° F. to 85° F. To prevent retrostasial congestion the patient's head is wrapped in a cold moist towel. The face is first bathed. The attendant then with one hand throws water from a vessel over the front of the body, and with the other, meanwhile, rubs the back. Colder water is used until the patient feels cold; should his teeth chatter he should be immediately taken from the bath. A warm dry sheet, previously prepared, is then folded about the patient, and with it he is dried.

Affusions.—Water at a temperature of 50° F. to 65° F. is poured from above on the patient, who sits in the empty tub, or lies on a rubber cot. The degree of stimulation is in proportion to the temperature of the water employed, and the height from which it is allowed to descend upon the subject, i. e., the lower the temperature, and the greater the height, the greater the stimulation. This treatment should be very quickly given. In acute cases the patient sits or lies; in chronic cases he stands in water at a temperature of 100° F.

By means of the affusion the sensory cutaneous nerves over a large area are mechanically and thermally stimulated, and a reflex action on the heart, respiration, and metabolic functions ensues. The intermittent nature of the stimulation increases the effect produced.

Affusions should be used with caution, with precision as to temperature, and with due regard to the patient's power of reaction.

The Sheet Bath.—A rubber sheet and a blanket are laid on one side of the bed, or on an adjoining bed. There should also be in readiness several linen sheets, coarse or fine, according to the effect desired, a tub of water, a cup, and a sponge. The linen sheet is wrung out of water at 50° F. to 80° F., spread quickly on the rubber sheet; the patient, whose head and face have been bathed in ice water, and whose head has been wrapped in a cold wet towel to prevent retrostasial congestion, is laid on the sheet. Systematically, small areas of the body in succession are warmed by gentle friction. As soon as a part is heated a cup of cold water, 50° F. to 60° F., is poured on it. This procedure is continued till the patient feels cold or shivers markedly. Sometimes the subject is permitted to remain in the wet sheet for half an hour; then often a gentle sleep follows. The first effect of the cold wet sheet is to contract the peripheral vessels; next dilatation of the cutaneous vessels occurs and is aided by the friction; the cold water then again contracts them; and so the process continues.

Drip Sheet.—The drip sheet is a modification of the sheet bath. The room in which this measure is carried out should have a temperature of not less than 70° F. The patient, with a wet towel on his head, stands in

12 inches of water at 100° F. A dripping sheet, wet with water at 75° F., is placed over his shoulders; under the right arm, across the back, over the left shoulder, across the front, and over the right arm. Quick strokes and occasional slaps are made by the operator up and down over the sheet. Twice or thrice during the procedure a basin of water, 10° F. or 15° F. colder than the water in which the sheet has been dipped, is poured over the head and shoulders of the patient; in the intervals friction for 5 to 10 minutes is applied. On removing the sheet—which should be rapidly done—the skin is hyperemic. The patient then steps out upon a woollen rug or blanket, is completely dried with soft linen towels, and then rubbed down with a warm sheet or towel. If this bath greatly fatigues the patient, its duration should be lessened till the reaction and resistance are strengthened.

The strength of stimulation in this measure may be greatly varied by varying any one or more of the factors, temperature, friction, the use of coarse or fine sheets, the use of the sheet dripping or well wrung out, the frequency of the applications of cold water during the process, and the duration of the bath. If the hands and feet are cold even on arising, it is well to induce heat to accumulate before the sheet bath is given, by piling on blankets, by giving a wet pack for ½ to one hour, or by a vapor bath for a few minutes.

The Cold Rub. The Cold Sponge.—On arising, before losing the heat of bed, the patient is wrapped in a sheet well wrung out of water, temperature 60° F. to 75° F., and is very actively rubbed down, with frequent slapping to produce an active hyperemia of the skin. After rapid drying and the administration of a cup of hot milk the patient is sent out for a walk.

The Wet Pack.—A rubber sheet is covered by a large blanket, which hangs over one side of the bed and down over its foot. A large coarse sheet, very well wrung out of water at 60° F. to 70° F., the temperature being varied to suit the case, is spread on the blanket. The patient, his head in a wet turban, lies down with upstretched arms; the right side of the sheet is brought under the arms across the front of the body, and between the lower limbs. The left side is brought over the arms and body and tucked in at the neck and feet. The blanket is then drawn firmly about the patient and tucked in at the sides, neck, and feet. "Everything depends upon complete exclusion of air from beneath the blanket cover." If the patient is chilly he should be covered with blankets. Partial packs, including only the body below the axillæ, may be given. The pack lasts ½ to one hour. The effect varies with the duration, the texture of the sheet, the temperature of the water, the extent of the pack, and the frequency and number of times it is repeated. To restore the tone of the cutaneous vessels, which have been relaxed by the wet pack, the half bath, the sheet bath, or the cold ablution should follow. In the wet pack the

reaction is entirely dependent upon the patient's capacity. If the skin be previously warm the reaction is better. The power of the patient to react should be tested and educated by other hydrotherapeutic measures before wet packs are given.

In the cold wet pack there is an initial shock lasting from 5 to 20 minutes. This is followed by a hyperemic cutaneous reaction. There is an interchange between the cooled blood of the peripheral circulation and the warm blood from the viscera, which continues until the sheet is thoroughly warm. The excretion of the skin is increased, and toxins are eliminated. The wet pack also has a calming effect due to withdrawal of blood from the brain and the exclusion of external cutaneous stimuli. To secure the antipyretic action the water for the initial pack should be 60° F. to 70° F. When the first pack is warm the patient should be put into another, wet with water 2° F. warmer. As soon as the second pack is warm the procedure may be repeated, raising again the temperature of the water employed 2° F. This is done till 4 or 5 packs have been given, or until the body temperature be satisfactorily reduced. If the pack be given for its sedative action and sleep follow the patient should be permitted to remain in the pack till he awakes; a cold ablution should then be given.

Hot Blanket Pack.—Three or four blankets are laid on the bed; one blanket is wrung out of water as hot as can be borne by the hands, and spread on the bed. The patient is folded in this, and covered by the other blankets. After a cold wet pack the sheet is warm; but after a hot blanket pack the wet blanket is cool, showing that there has been a diminution of heat production.

The Wet Compress.—Almost all forms of the compress consist essentially of a linen basis, which is the vehicle for the application of the water, and a dry flannel bandage which covers and secures it. These vary only in shape and size to suit the region of the body to which they are to be applied, and in the temperature of the water used.

The cold compress causes contraction of the peripheral vessels, and should, therefore, be renewed frequently enough to keep it a cold application. When the stimulating compress is employed the water is at 60° F., and the compress is permitted to remain *in situ* till it is warm or even dry. When covered with waterproof material the compress becomes a surgical wet dressing; astringents or alcohol are often used for wetting. It is so difficult to keep water compresses hot, and so inconvenient to handle them, that better heat-retaining media, such as the linseed compress, are much used.

If the temperature of the patient be high the compress should be changed every ½ hour; otherwise every hour, night and day, unless the patient is asleep. Fresh water should be used, and the compress boiled every day to prevent septic infection of the skin.

The Abdominal Compress.—The linen used for this compress should be in three layers, of sufficient width to extend from the xiphoid process to the symphysis pubis, and fall over the sides of the trunk. The water out of which this cloth is wrung should be at a temperature of 60° F. to 70° F.

The Neptune Girdle.—The Neptune girdle is a modification of the above compress. The linen is made long enough to encircle the body and form a double fold on the abdomen. It is covered by a dry linen or flannel binder, and is changed twice or thrice in the 24 hours, the part being sponged with cold water before each renewal.

The Combination Compress of Winternitz.—The Neptune girdle is applied as described. A Leiter coil, arranged to have hot water passed through it, is laid on the epigastrium. This hastens the reaction, and reflexly stimulates the nerves of the underlying organs. When a compress is employed to reduce inflammation it should be frequently changed, never being permitted to become warm. The object here is to keep the vessels of the inflamed part in a state of contraction. The temperature should not be so low as to paralyze the cutaneous vessels, nor so high as to dilate them. To attain the desired end a temperature of 50° F. to 60° F. is suitable.

Cold Applied to the Head.—Instead of using the clumsy ice bag, which wets the pillow, a wet cloth may be laid on the head, and held in position by a cap of coiled rubber tubing through which ice water flows.

The Full Bath.—This may be given hot or cold, with or without friction. The cold full bath has become intimately associated with the name of Brand in the therapy of typhoid fever. Brand's method for the cold full friction bath is described later.

Another form of the cold full bath is the graduated bath of Von Ziemssen. The patient is placed in a tub which is partially filled with water at a temperature of 86° F. to 90° F., and to which water of a temperature of 40° F. is added till a temperature of about 77° F. is attained. Friction is used, and the bath lasts ½ hour. The patient, on emerging, is allowed to remain in warm blankets for 15 minutes before he is dried and dressed.

Winternitz recommends the employment of alternate half and whole cold baths, the former at a temperature of 60° F. to 68° F., the latter at a temperature of 42° F. to 50° F. The patient remains in the half bath 1 to 2 minutes, then steps into the other for ½ to 1 minute, continuing the alternation according to the extent of the desired reaction.

As a hydriatic measure the cold full bath requires the strongest reactive response from the patient; it is therefore necessary, especially as the reactive power is weakened in the sick, to bring to its aid the friction insisted upon by Brand and his followers.

The Cold Plunge.—This bath should not be entered if the subject feels chilly. If necessary the skin should be previously warmed by some other procedure, such as the wet pack. The face and neck should first be bathed with very cold water, and the plunge bath then entered suddenly. The whole body should be immersed in the water, the head also being dipped several times. The bather should exercise, or rub himself in the water. The plunge bath should last from a few seconds to 2 or 3 minutes. It should be followed by vigorous rubbing. As soon as dry the patient should exercise moderately, or be massaged.

The Warm Full Bath.—Any bath with a temperature above that of the skin (92° F.) Baruch designates a warm bath.

The temperature of the room in which a warm bath is given should be between 70° F. and 80° F. Warm towels and a warm sheet and several hot-water bags should be in readiness. If there is no hot water on tap, tubs of water at a temperature of 200° F. should be prepared, so that the bath temperature may be raised at any time if necessary. The water in the bath should have a temperature of 95° F. (Baruch); it is also used at temperatures between 98° F. and 104° F. The patient wets his face and neck with the water in the tub before entering it. He lies down in the bath and should remain immersed to the chin. The duration of the bath varies with the conditions for which it is administered. Something warm should be provided for the patient to step out upon; the warm sheet is rapidly folded around him; and he is put into a warm bed and covered with blankets. After a few minutes he is dried. Profuse perspiration is to be avoided.

When the bath is warm the irritability of the sensory nerve endings is decreased; the bath has therefore a sedative effect. A hot bath—one above 100°—has a directly opposite action.

The Continuous or Hammock Bath.—The ordinary bathtub is not suited for this purpose. So that the patient may be able to repose in comfort for a prolonged period he is suspended in a hammock-like arrangement, which should clear the bottom of the tub. Suitable rests should be provided for the head and nates. The temperature of the water should be 95° F. to 100° F. The water may be changed once in 24 hours, or a constant inflow and outflow may be arranged. Before the patient enters the bath his skin is anointed with a fat—lanolin or vaselin—as saturation may cause shriveling and peeling. It is desirable to have the tub raised from the floor and covered with blankets to exclude air and prevent exposure. A wooden board may be placed across the tub to serve this purpose, and also as a tray for the patient's meals. The patient may be lifted from the tub to evacuate the bowels and bladder, or the urine and feces may be permitted to pass quickly away in the outflow. A patient is kept in the continuous bath for any length of time, from a few hours to more than a year. This measure acts by the removal of all external irri-

tation of the cutaneous nerves, and by protecting the surface of the body from atmospheric changes.

Localized Baths.—Various forms of tubs have been devised for localized continuous baths of the arms and legs.

The Effervescent Bath.—For the Nauheim bath see Vol. III, Sec. III, Chapter II.

Douches.—In the douche a column of water descends from a height. There is thus obtained the mechanical action of the pressure of the water as well as the effect of its temperature. Many forms of the douche exist. The vertical rain douche is a shower bath, in which the water falls from a perforated nozzle or rose. The jet or fan douche is a movable arrangement to direct a column of water upon any part. The ascending or perineal douche is a spray of water, directed upward, over which the patient sits on a stool with a ring-shaped seat. In the circular douche the water is directed horizontally inward from circular tiers of perforated metal tubing. The Scotch douche, or alternating douche, applies heat and cold alternately, either live steam and cold water being alternated or warm water being used in place of the steam. Carbon dioxid and hot air are also applied by means of douches. As these are measures which are mostly practicable in institutions only they will not be further considered here.

Hip or Sitz Bath.—The tub used for this bath is familiar. The temperature of this bath is varied; it may be cold, tepid, warm, or hot. There should be enough water to reach to the umbilicus of the patient when he is seated in the tub. The patient should be carefully covered to protect him from chilling. Friction of the upper part of the body may be added to this treatment. The sitz bath acts on the abdominal and pelvic organs and vessels, its action depending, as in other forms of baths, on the temperature of the water and on the duration of the bath. Other partial baths are the occipital bath, the elbow, the hand, and the foot baths.

The Occipital Bath.—The patient lies down with the head immersed for 5 to 10 minutes in a vessel through which tap water is flowing.

The Elbow Bath.—The elbow is kept in a vessel of running cold water for 10 to 20 minutes. Hand and foot baths are given in the same way, but the water may be used cold or hot.

Application of Extreme Temperatures.—*Steam and Hot Air Baths.*—These are commonly given in cabinets which inclose the entire body with the exception of the head. The head and neck must be cooled during the bath. The temperature of the bath, usually 104° F., though possibly higher, is attained gradually as the steam enters. The duration of the bath varies with the indications, rarely being more than thirty minutes. Winternitz has devised a method for a steam bath at home. A wooden raft-like frame lies at the bottom of the tub on which the bather is raised from the floor of the tub. A continuous flow of hot water gives off steam

in the tub, which is well covered to prevent its escape. Higher temperatures can be borne in hot air than in steam baths, and in steam than in hot water. The bath causes rapid dilatation of the cutaneous vessels, followed in a few minutes by sweating. To increase the perspiration cold water is given to the patient to drink. It is best after the bath to employ some cooling hydriatic measure.

Russian Bath.—The Russian bath is a form of steam bath.

Irish-Roman Baths.—Irish-Roman baths are hot air baths, where the patient enters a series of rooms filled with air of increasingly higher temperature.

Ice.—The most common way of applying extreme cold is by means of the ordinary ice-bag; the use of coiled tubing, the Leiter coil, through which ice-water is passed, is, however, preferable. The tubing is coiled in any form to fit the part to which it is to be applied. The ice cradle is an ordinary hospital cradle, placed over the chest, abdomen, or entire body. The patient is stripped. Ice-bags or pails of ice are hung from the pole of the cradle, and the whole covered over with a thin sheet. The patient is kept in the ice cradle till his temperature is sufficiently reduced. A hot-water bag is kept at his feet to prevent chilling.

Ice Rub.—The ice rub is given by means of a flattened piece of ice in a cloth with which the parts of the body are rubbed in succession.

Ice Pack.—The patient is stripped, and enveloped in a cold wet sheet. An ice cap is laid on his head, and pieces of ice, carefully swathed, are placed at his sides. He is rubbed by the nurse with pieces of ice, as in the ice rub. Other methods of using extreme temperatures are the ether and ethyl chlorid sprays and the application of carbon dioxid snow.

General Summary.—Measures which may so markedly influence vital processes as do these hydrotherapeutic applications, are extremely valuable therapeutic agents, but if skill, precision, and judgment be not employed in prescribing and applying them they may be productive of equally great injury. Local applications of heat or cold have little influence on general somatic conditions, and find no contraindications in any such conditions. Local heat should not be applied for the reduction of a circumscribed inflammation, as it raises the temperature of the inflamed part, and increases the formation of pus; cold, however, by lowering the temperature, and reducing the number of pus cells, and the congestion, may check the inflammatory process. As an analgesic measure either may be effective; trial decides which should be used. Cold applied to the head is a precautionary measure in any general application of cold or heat to prevent what Winternitz calls "retrograde hypostatic congestion," i. e., the flow to the head of the blood driven from the stimulated surface; this may be dangerous in arteriosclerosis. General cold applications should never be given in states of exhaustion or nervous debility; or in collapse with subnormal temperature; during a chill; or during a hemorrhage. The pa-

tient should be previously warm; though, in tuberculosis, Aberg advises the giving of cold full baths without preparation of the patient. Full baths of too high or too low temperature should be avoided in cardiac disorders, and any general applications should here be used with great caution. In conditions of cerebral hyperemia, such as exist in apoplectic individuals, warm full baths are contraindicated. In all these procedures, where there is any suspicion of reactive weakness, the reactive capacity of the patient should be trained by the use of gradually increasing stimulation, regulated by changing the duration, temperature, and accompanying mechanical stimulation. Bathing in natural bodies of water, such as the sea, rivers, lakes, etc., should be prescribed in accordance with the existing conditions of temperature and stimulation by the motion of the water, and with regard to the strength of the patient.

More specific treatment of the indications and contraindications for the various hydrotherapeutic measures is given in the next chapter.

Special Hydrotherapy

Diseases of the Circulatory System

The hydrotherapy of circulatory diseases is very simple. Through stimulation of the cutaneous nerves by means of waters charged with salts and gas, or turpentine, or ammonia, or other mild irritant, vasoconstriction is produced in one set of arterioles, and a vasodilatation in another. Conceivably also the stimulation reflexly influences the heart muscle itself. The vasomotor changes produce endocardial stimulation by raising the blood pressure. But together with the rise there is dilatation of the visceral arterioles so that the blood is driven into and through the stagnant parts of the circulatory system. The nutrition of organs in which stasis is a menace is thus improved. The heart is made regularly, mildly, and effectively to act. The coronary capillaries may share in the blood redistribution and the heart thus benefit directly from the bath. But there is as yet no proof of any special implication of the coronary circulation. Doubtless, however, cardiac nutrition is enhanced by the steadying and slowing influence of the discreetly increased blood pressure. It is, as it were, a mild and beneficial exercise which the heart enjoys. The slowing of the rate and of the cardiac rhythm not only enables the heart effectively to empty its cavities, but in the prolonged diastoles an opportunity for regular and systematic flooding of the coronary capillaries occurs, and the nutrition of the heart muscle improves.

The application of cold to the precordia will slow the rapidity of an irritable and infected heart. It is a valuable adjuvant to the treatment of endo- and pericarditis, as it moderates the fevered activity and saves

the cardiac muscle from undue exhaustion. Moreover, in valvular lesions, this tranquilizing of the heart spares the fragile, edematous, infiltrated valves from as many impacts as the beats that are avoided. Precordial cold applied causes also a dilatation of the vessels in the heart muscle and in the pericardium, and thus aids in repelling the bacterial invasion by augmenting the blood supply.

Heat applied to the precordia stimulates the heart to more forcible, more regular, and more efficient contraction. It, also, reflexly, causes a constriction of the coronary vessels. In weak, distended, dilated hearts the application of heat acts as a powerful stimulus and soon strengthens, regularizes, and increases the amplitude of the pulse, and diminishes the area of cardiac dulness.

Arteriosclerosis.—It is of great importance to recall the dual relation which the increased peripheral resistance maintains in this common malady. It serves, not only as a cause, but also as an effect. When faulty dilatation of the vessels exists there ensues an imperfect elimination of unknown products of metabolism which lead to a toxemia. This increase of circulating toxins mainly by direct action on the vessel walls, but perhaps indirectly also, through the vasomotor nerves, gives rise to a spasm of the vessels which, in turn, leads to a still more scanty blood flow; as elimination is dependent upon the rate of renewal of the blood in the emunctory organs, such a decrease in the vascular supply serves to cripple depuration still more. Thus a vicious circle is instituted and the toxemia increases. The origin of the noxious metabolic products may be putrefaction in the intestinal tract. The increased resistance to the vascular current in turn places added work upon the heart, which at first hypertrophies and later frequently dilates as myocardial changes occur. As, except for temporary effect, drugs should not be given to obtain the desired vasodilatation, hydriatric measures possess a particular value in the treatment of sclerotic vessels. By hydrotherapy it is possible to reduce the undue constriction of the vessels, thus to augment the blood flow and to promote detoxication or elimination. The partial rub with a temperature of 68° F. is best suited to be the initial measure. If the patient withstands this mild procedure, after a few days, more stimulating measures, such as the full cold rub, preferably at a low temperature, should be instituted. In cases of extreme illness the rub may be given at 68° F. for several days and gradually water of a lower temperature introduced. The duration of the rub is governed by the reaction. The applications of cold to the precordium and spine are indicated not only to meet the effect of the disease on the circulatory mechanism, but also to counteract the added strain placed thereon by diaphoretic measures. The steam bath of moderate duration and temperature, not exceeding 140° F., followed by a heat-abstracting measure, is employed, but must be conjoined with cold applied to the precordial region. The employment of the hot bath, 95°-

100° F., is of great service. Venous sluggishness yields often to running foot baths.

Endocarditis.—*Acute Endocarditis.*—In all cases of acute endocarditis the application of cold to the precordium is indicated, as by this measure cardiac sedation is secured and the possibility of the occurrence of embolism is minimized. The applications of choice are the precordial coil and the ice bag. The selected one should be kept in place continuously for a period of, say, several days, unless the heart shows signs of weakness. In the presence of non-inflammatory myocardial changes cold precordial applications must be used with caution or not at all. Partial rubs later in the course of the disease are advocated.

Chronic Endocarditis.—Local stimulation of the heart obtained by the use of the cold precordial coil is practiced. It is claimed that digitalis may be supplanted by this application. The use of heat to induce general invigoration and to reduce peripheral resistance is advisable, but only under extreme caution, as the temporary increased activity resulting from thermic measures may be most potent in producing cardial dilatation. Diaphoretic measures, as wet packs, partial rubs, and the Winternitz modified steam bath applied five to ten minutes, are of value in reduction of edema. The last consists in exposing to steam the lower parts of the body while to the precordium is applied a cold coil to reduce the danger of dilatation. Irregular or broken compensation and cardiac insufficiency require careful hydriatric management. Much depends upon the changes in the heart muscle. The use of the carefully graduated partial ablution (68° F.) for several days and then the application of the cold precordial coil are the usual treatment. If there be undue vascular constriction present in the cardiac insufficiency general measures may be applied to eliminate it.

For the Nauheim treatment see Diseases of the Myocardium, Chapter II, Sec. III, Vol. III.

Hemorrhoids.—This aggravating malady often yields to brief, cold sitz baths of about 85° F. temperature. Hot hip baths are also advocated. Should inflammation arise, the duration of the sitz bath may be increased.

Acute Pericarditis.—The ice bag or cold Leiter coil are applied continuously to the precordium with the same precaution observed in acute endocarditis. These measures exert decided analgesic and anti-inflammatory effects. Hyperpyrexia is treated with extremely cold half baths. Diaphoretic measures, particularly the wet pack for two hours, are indicated by an obstinate effusion.

Diseases of the Respiratory Tract

Asthma.—A brief application of cold to the nape of the neck effects relief in bronchial asthma depending upon nasal conditions. The form used may be an affusion, or a douche under ten pounds pressure.

Acute Bronchitis.—A wet pack for two hours, followed by mechanical stimulation, should be tried in an attempt to terminate the disease at its onset. The cross-pack (Priessnitz) at a temperature of 45°-55° F., renewed every two hours, often lessens the cough and exerts an analgesic effect. The Lissauer method of spraying may be employed for its expectorant influence: after rapid application of a steam spray at 110°-125° F., for fifteen seconds, over the upper part of the trunk, a cold fan douche is applied for three to five seconds; a rapid friction rub follows. In sixteen cases in which this routine was employed Lissauer obtained ready expectoration. The cold Leiter coil to the precordium may be needed, particularly in the aged. Hot mustard foot baths are of proven value.

Acute pulmonary affections frequently complicate the exanthemata, particularly measles. When in their course, bronchitis or bronchopneumonia appears, cold half baths for five minutes at 78.8°-71.6° F., with douching and subsequent gentle mechanical manipulations, are indicated. Extremely brief plunges into water at 61°-54° F., succeeded by strong friction, may be used if the case is doing badly. The mustard pack as practiced by Herzfeld is very efficient. In this measure flannel applications are made of one to ten or twenty dilution of oil of mustard which has been made according to the directions of the German Pharmacopeia. The diluent is equal parts of alcohol and water and the degree of dilution depends on the urgency of the case. The application envelops the child from the neck to the knees and remains in place until the skin is markedly hyperemic. When the desired cutaneous hyperemia is attained, usually in from fifteen to thirty minutes, the child is placed in a wet, thirty-three per cent. alcohol pack. At the expiration of one half hour the wet pack is supplanted by a dry sheet. This procedure should be repeated every twenty-four hours and oftener if the case is very severe. It produces its happy results very rapidly.

Edema of the Lung.—The mustard pack is claimed to be quite efficient in pulmonary edema. The application is continued thirty minutes.

Hyperemia of the Lung.—The hot bath at 106°-110° F. for ten minutes or the hot bath for five minutes followed by a warm pack, is the usual remedial measure employed. The hot mustard foot-bath is of value to induce sweating.

Pleurisy.—In acute pleurisy three symptoms are present, cough, dyspnea, and pain, which are amenable to hydriatric treatment. The cross-binder through which passes a cold water coil is the most efficient measure. The ice bag may be used. Wet packs and mechanical stimulation, and half-baths, 71.6°-68° F., are valuable auxiliaries. In event of an effusion steam baths or hot air baths, lasting ten to fifteen seconds, followed by invigorating measures, are employed to induce diaphoresis. The two hourly-changed cross-binder may aid absorption of an effusion. Should

respiratory or cardiac embarrassment appear the cold precordial coil is indicated. High fever is controlled by wet packs.

Constitutional and Metabolic Diseases

Anemia.—*Chlorosis.*—To prevent heat abstraction while obtaining energetic stimulation of the nervous system is the hydrotherapeutic aim in treatment of chlorosis. To lessen the heat loss, all cold applications should follow some heat-retaining measure, such as the warm bath at 100° F., with room temperature not below 70° F., the dry pack; or, without increasing the heat by additional measures, the heat retention during the period of sleep may be utilized by applying the invigorating procedures upon arising in the morning.

The choice of the innervating measures is great. Ablutions of 80° F., which are lowered two or three degrees daily and combined with mechanical stimulation rapidly given in the warm bath, frequently give happy results. The ablution may also follow the dry pack. Wet packs followed by the half bath and rain baths are valuable auxiliaries, when the nerve tone has been heightened. Circular and spray douches of two to thirty seconds' duration, with water, first of high temperature, 95° F., and then reduced to a temperature as low as 45° F., followed by massage, yield excellent results. Hot-air baths of 125° F. to 160° F. should precede the use of the douches.

The following plan of treatment is valuable: Electric light baths for fifteen to twenty minutes, then the fan douche at 105° F. with twenty pounds pressure for thirty seconds, and then at 70° F. for fifteen seconds, and a dry rub, followed by one hour of rest. This treatment is repeated on alternate days.

Secondary Anemia.—The general treatment is that prescribed for chlorosis. Among the special manifestations of the paucity of the blood cells, the cephalalgia, and the coldness of the extremities—particularly the feet—may require special measures. The headache responds happily to the use of a hot-water coil applied to the neck, and the cold rub confined to the legs. Brief running foot baths are the most efficient measure to relieve the coldness of the feet. Cold douches used after a preliminary hot application are indicated in anemia of the viscera. They may be general, as the Scotch douche, or localized, as the fan douche applied to the abdomen.

Diabetes Insipidus.—Warm or cold half baths and full baths are recommended. The half baths possess a special value for neurotic children.

Diabetes Mellitus.—In addition to attaining a strict cutaneous hygiene, thus obviating the dangers of cutaneous complications, hydrotherapy

exercises some remedial power over diabetes, especially that form which accompanies obesity. Powerful stimulating measures are employed and are often preceded by the application of heat. All efforts should be concentrated upon the attainment of a vigorous reaction. Improved general metabolism and lessened tendency to acidosis are among the beneficial results obtained by the use of water.

The hot air or electric light baths for five to ten minutes, next the circular douche, 105° F., for thirty seconds, then continued at 90° F. for thirty seconds, and then the jet and fan douche to the entire body, 70° F., for twenty seconds, may be employed once every twenty-four hours. The temperature of the final water should be gradually reduced until 60° F. is reached, and the jet douche pressure should be progressively increased until twenty or thirty pounds is attained. Ten-minute half baths at 85° F. with vigorous mechanical stimulation while in the tub, preceded by wet packs, may be used. The packs should be continued about forty-five minutes, and should be, when applied, about 50° F. Brief cold plunges and the dripping sheets accompanied by friction may be employed at home.

Exophthalmic Goiter.—Applications of cold, either the Leiter coil or ice bags, to the thyroid gland and the precordium serve to slow the heart. Occasionally an ice rub may be needed. Wet packs for one hour, combined with the cold Leiter coil to the spine, and followed by a half bath, 79° to 75° F., sometimes allay the tremor and palpitation.

Obesity.—The attempt of hydrotherapeutic measures in treatment of obesity is to increase general metabolism and thereby promote oxidation. In the presence of fatty myocardial changes the more severe applications should be made with caution, or with a cold precordial coil. Diaphoresis by means of hot air baths, electric light baths, steam baths, full hot baths, and packs, of ten to forty minutes' duration, should be induced. Then cold applications in the form of half or full baths, douches, and rubs, at between 55° F. and 70° F., should be employed. Frequently an alcohol rub concludes the treatment. Hinsdale finds the combination of full hot bath and pack superior to that of hot air bath and douches, and cites two hundred and sixteen cases in which this combination was used. Of these cases one hundred and sixty-eight gained weight. Together with a strict dietary régime and hydrointervention, muscular exercises should be rigidly enforced. Physiologically unfamiliar exercises are the movements of choice. While each case presents peculiarities necessarily entailing modifications in the treatment, the following prescription from Hinsdale may be followed as a guide: A full hot bath at 104° F. for twelve to eighteen minutes during the first three days. A hot dry pack is then applied for the same length of time. A cool spray, about 75° F., and an alcohol rub are the final applications. After a short rest of twenty minutes long walking exercises are instituted, and massage for one hour

follows their termination. Some advocate the application of heat only to a degree necessary to obtain visible perspiration.

Podagra.—When gout is found in association with obesity the hydriatric management laid down for that disorder should be installed at once. In the more acute forms analgesia with minimization of the articular and periarticular effusions may be obtained by the use of brief cold applications to the affected parts. These may be followed by circular cold compresses. To combat the more chronic gout the following treatment may be employed: A jet douche of 104° F. under fourteen to eighteen pounds pressure is followed by a full bath at 100° to 104° F. The patient is then placed in a dry blanket pack for ten to twenty minutes, and then given a cool douche. A rapidly administered alcohol rub ends the treatment. The indirect douche at a temperature of 98° to 104° F. applied under a force of fifteen pounds in a warm bath is also employed. Wet packs applied from one to two hours, with a subsequent brief cold douche, such as the rain douche, are of value. General diaphoretic measures, such as the hot air bath until perspiration is visible, followed by gradually lowered pressure douches, are warmly endorsed. The success which the spa treatment of gout has met seems to rest in part upon the severe hygiene there imposed upon the patients, as the hydriatric values of the various waters seem no greater than that employed in the hospitals and sanitaria.

Chronic Articular Rheumatism.—If in good condition the patient should be placed in the hot air cabinet for ten to fifteen minutes, after which the jet douche should be applied, at thirty pounds pressure, if the tenderness is not extreme. The hot air water douche at 110° to 115° F., and the cold douche at 80° F., alternating with one another for fifteen and thirty-second periods of application respectively, until three or four minutes have elapsed, are utilized. Another form of routine treatment is as follows: The patient receives a brisk rubbing while in the full bath of 102° to 104° F., which is continued eight to ten minutes. Upon leaving the bath he is placed in a hot dry blanket pack, in which he remains eight to twelve minutes. A five-minute alcohol rub concludes the procedure. Later a hot douche, 103° to 104° F., before the bath may be given. It should not be applied to the head. Massage and a cool douche after the bath may be employed.

Steam baths and wet packs may be of value. They should be followed by low temperature applications, as cold rubs or three to five-minute cold half baths. The Scotch douche and circular compresses applied locally are most valuable. It is possible by these various procedures to improve the circulation of the affected parts, cause absorption of effusions, and increase the mobility of the diseased joints. Atrophy of the surrounding muscles may be combated by massage or by the use of a very brief cold shower bath to the part in question. Faradization of the joints for a

short time, ten to fifteen minutes, enables the patient to withstand greater mechanical stimulation.

Muscular Rheumatism.—The most common varieties of muscular rheumatism are lumbago, pleurodynia, and torticollis. For these hot dry packs, with moderate mechanical stimulation, may be employed with happy results. Baruch recommends the use of the hot air cabinet for five to fifteen minutes, followed by the pressure jet douche. The pressure should be thirty pounds unless much tenderness be present. Should the condition tend toward chronicity, alternating temperature applications will prove of value.

Diseases of Genito-Urinary System

Bladder.—*Cystitis.*—Inflammatory processes of the bladder may be treated by prolonged baths and irrigation. The bath is usually given at a temperature of 100° F., and is continued for eight hours daily. While the bath is given the bladder is continuously irrigated. Hunner reports six cases of bladder disease as favorably influenced by this treatment. Warm sitz baths, 86°-90° F., for thirty to sixty minutes, are recommended. The hammock bath at 95°-100° F., applied hours daily for a long period of time, even months, often affords relief. But the inconvenience and trouble involved are hardly repaid by the results.

Nocturnal Enuresis.—Affusions at 60° F. and the half bath are recommended. Cold rubs and cold plunges at 60.8°-64.4° F. are of value to effect restoration of the lost sphincter tone. If these measures are not fruitful, the short cold sitz bath may be tried.

Kidneys.—*Acute Nephritis.*—Gentle diaphoretic measures are indicated in acute nephritis. Moderate sweating can be secured by the use of hot baths, 100°-108° F., lasting from fifteen to thirty minutes. The effect of the baths is prolonged by the use of a dry blanket pack after the bath. Moderate diaphoresis is highly desirable, as it places less strain on the heart and lessens the danger of uremia due to sudden elimination of a large portion of the liquid portion of the blood. Such treatment is based upon the assumption that the skin may partly assume the renal excretory rôle. This view is not entertained by many noted scientists, who claim the excretory function of the skin is so slight as to be practically negligible. It may be that the warm baths increase the toxin destruction or its modification or its elimination by the kidney and bowel. For the nephritis of febrile diseases, particularly that of scarlatina in infants and in the extremely young, the warm bath, 100°-101° F., is used; for older children full tub baths at 90°-100° F., with the child in a blanket, render best service. Half baths at 73°-77° F. combined with strong dry rubs are recommended. Copious drinking of alkaline waters augments the results obtained by these measures.

Chronic Nephritis.—The treatment of chronic nephritic conditions is mainly diaphoretic. This is particularly true in the cases of interstitial nephritis. As a rule, the diaphoresis is more rigorous than in acute nephritis. Hot and cold applications are employed. Of the former one may select the hot bath, the steam bath, the hot air bath, or the electric light bath. Dry heat is less effective than moist. If there be pronounced sclerotic changes in the arteries the baths must be given cautiously. The application of the cold Leiter coil to the precordium will quiet the heart during the period of thermic excitation and guard against cardiac weakness. The electric light bath, in thirty-minute applications, followed by a blanket pack, has given excellent results in nephritis with edema.

The following measures may be employed in the order given: The electric light bath for ten minutes, followed by a circular douche at 102°-106° F., at twelve to fifteen pounds pressure, for thirty to forty seconds; then the jet douche at the same temperature and pressure applied for thirty to forty seconds; finally, vigorous dry friction. Baths at 95°-100° F. may be used in subacute cases. All these hydrotherapeutic measures must be combined with dietetic treatment, especially restriction of fluids.

If the rigid vessels can withstand the initial stimulation caused by the shock of cold applications, the cold douche, the cold rub, cold baths, and the cold pack may be used. Continuous packs at 70° F. over the loins and abdomen, changed every five hours, coupled with baths at the same temperature, are highly recommended.

The effect of hydriatric applications is to increase the percentage of urinary solids. This increase may persist for several days after the application. The cold measures are most effective in augmenting the volume of the urine.

Uremia.—Hot wet packs applied for thirty-minute intervals every four hours, and vapor baths, given by covering hot bricks with wet cloths, continued for an hour, are employed. Careful enteroclysis with water at a temperature of 110°-120° F. may be tried when all else fails. Eclamptic manifestations sometimes yield to the wet pack at 70° F. applied for one hour. Alcohol sweat baths are of value. The withdrawal of blood up to one liter should not be delayed. If it be possible to obtain a strong reaction, cold in the form of half baths at 68°-71.6° F. or cold wet packs at 70° F. are utilized.

Prostate and Urethra.—*Acute Gonorrhea.*—Local thermic applications are recommended in gonorrhea. The usual form employed is immersion in water at a temperature of 105°-115° F. for ten to fifteen minutes three or four times a day. Local cold measures are also endorsed.

Gonorrheal Arthritis.—See Joint Affections.

Prostatitis.—Continuous irrigation, as described under cystitis, possesses special value in relieving prostatic diseases. The water used in the acute form may be cold, that is, at a temperature of 50°-53.6° F. Care must be exercised to avoid increasing vesical irritation, which is often present. Chordee may be relieved by the hot hip bath.

Salpinx-Uterine-Ovarian.—*Amenorrhea.*—Amenorrhea is usually accompanied by a relatively scanty blood supply to the uterus. Its correction is usually achieved by hot local applications. Hot sitz baths at a temperature of 110°-114° F., lasting ten to thirty minutes, and the hot vaginal douche at 105°-110° F., are the measures most often utilized. Hot full baths may be pressed into service. The benefits accruing from the employment of these procedures may be increased by general massage in all cases, and in a few specially indicated cases by the kneading of the pelvic tissues. Later, measures to increase the systemic tone may be adopted.

Dysmenorrhea.—If spasm of the uterus is found accompanying painful menstruation, hot applications are efficacious. Those of choice are the hot sitz bath before retiring, hot douche, and hot compresses. The range of temperature should be from 108°-115° F. Nauheim baths are recommended by Baudler. If the dysmenorrhea is due to faulty nervous mechanism, general measures should be instituted to reëstablish the normal function.

Chronic Endometritis.—To increase the vascular tone and remove the excess of blood a vaginal douche at 108°-115° F. should be given both upon arising and just previous to retiring. One to two and a half gallons of water should be used, to which enough salt should be added to determine a physiological saline solution. Excellent results are yielded by the Nauheim treatment if but little connective tissue overgrowth has occurred. Short cold sitz baths at 85° F. may be tried. During gestation the hydriatric measures should be employed with extreme caution.

Menorrhagia.—Of the local applications designed to lessen profuse menstruation, the long continued vaginal irrigation at a temperature of 120° F. produces excellent results. In addition general and local measures directed against the causal factor should be installed. Extreme cold in the form of cold vaginal douche and ice applied intravaginally and cold rubs, is used.

Chronic Metritis.—This is rarely found except as an accompaniment of endometritis. Nauheim baths are recommended for those forms due to incomplete involution and inflammation. In general, the treatment is similar to that of endometritis.

Acute Salpingitis.—The severe pelvic pain usually present may be modified considerably by prolonged vaginal irrigation. Two to three gallons of normal salt solution at 110°-120° F. should be used three times daily. Hot abdominal compresses are valuable adjuncts. If severe pain

yields not to these measures, the ice bag may be tried. Should the condition become chronic, the Nauheim bath will exert a desirable sedative effect upon the pelvic circulation.

Testicle.—*Epididymitis and Orchitis.*—Thick compresses wet in a saturated solution of magnesium sulphate at 60° F., renewed every half to one hour, lessen the pain and promote absorption of the inflammatory exudate.

Diseases of Gastrointestinal Tract

Biliary-Hepatic.—*Cholelithiasis.*—The chief value of the hydriatric measures in the treatment of gallstones is the relief of the paroxysmal pain of the biliary colic. Warm applications render the greatest service. The hot bath pack is highly recommended. This is applied as follows: The patient is placed in a bath tub and covered with water at 104° F., which is gradually increased to 115° F. The entire bath has a duration of five to ten minutes. When the bath is concluded, the patient is wrapped in a hot sheet and blankets and allowed to remain for thirty minutes to an hour. Then an alcohol rub or affusions at 60° F. is given. Hot water may be given by mouth and gastric lavage may be employed. The latter has proved effective in obstinate cases. The trunk compress with the hot coil often gives relief.

Hepatic Hyperemia.—Daily cold sitz baths at 46.4°-50° F. continued for five to ten minutes, and cold shower baths combined with cold movable fan douches to the skin over the liver often succeed in diverting the blood supply to the superficial tissues. The venous stagnation so frequently found in the liver is usually a manifestation of cardiac or pulmonary trouble, and is relieved by measures directed toward the improvement of the heart and lungs.

Enteric Diseases.—*Constipation.*—Constipation arising in the absence of organic disease is related to an atonic or spastic condition of the intestinal musculature. It is of highest importance to distinguish between these two forms, as the hydrotherapeutic management of each is radically different.

In the atonic form, general measures to invigorate and tone the faulty muscle should be employed. In patients of good physique cold may be applied at once, as a compress or douche. In the less heroic warmth to the point of perspiration is required prior to the administration of the cold applications. For atony one may proceed by applying the hot air bath or electric light bath until moderate diaphoresis is induced. This is followed by the circular douche at 95°-105° F., under fifteen to twenty pounds pressure, for one minute. The Scotch douche, with one-quarter inch nozzle and fifteen to twenty-pound pressure, is applied over the colon at 60° and 112° F. for fifteen-second intervals.

A fan douche at 75° F. and twenty pounds pressure, for ten seconds, to the back, abdomen, and chest, and massage to the abdomen with particular application to the colon, end the prescription. An open air walk augments the effects of the treatment. Irrigations of cold water at 64.4°-71.6° F., beginning with small amounts and later increasing to one quart are of value. The cold rub followed by a brief cold sitz bath of not over five minutes in duration, exerts a particularly happy effect upon the enteric neuromuscular mechanism.

The spastic variety of costiveness requires calmative measures. Warm or hot applications are more efficacious than are cold in effecting this desired relaxation and sedation. Warm or hot sitz baths at 104°-110° F. for twenty minutes, hot compresses to the abdomen, brief warm douches, and irrigation of water at 104° F. are the measures of choice. Carefully graduated cold enemas administered upon awakening have been advocated.

Diarrhea.—If purging be due to dietetic errors, the removal of the irritant material is imperative. This can be accomplished by cold hip baths, 50°-64° F., applied from one to five minutes. Irrigations are also of service. Should undue peristaltic activity be the cause of the diarrhea, hot sitz baths at 100° F. given from thirty minutes to one hour, the hot coil placed over the stomach in conjunction with a wet compress, and half baths at 100° F. are the indicated measures. The symptomatic diarrhea of catarrhal inflammation of the intestine disappears when the hyperemia, hypersecretion, and hypermotility are reduced to normal. This reduction may be realized by the intervention of moderately prolonged cold measures.

One routine plan is a cold rub, followed, without drying the skin, by a sitz bath at 50° F., for ten to thirty minutes. The abdomen receives a strong rubbing during the sitz bath. When the bath is ended an abdominal binder is put in place and replaced when quite dry. Another prescription begins with the hot air bath until the skin is hyperemic. This is followed by a wet sheet rub and a simultaneous hip bath at 70° F., and a foot bath at 110° F., for ten minutes. This may be given daily with gradual decrease in temperature of the hip bath to 50° F. The hammock bath at 95°-100° F. often has a benign influence.

Acute Enteritis.—After the contents of the intestines have been expelled, the severe pain and the diarrhea may be lessened by hot applications. Should chronicity develop, the half bath at 70° F. reinforced by the repeated pail-pour seems favorably to influence the course of the disease.

Acute Appendicitis.—The use of cold, as a cold coil, the ice bag, or an ice poultice, prior to operative interference lessens pain, emesis, and singultus. A protective gauze application should intervene between the skin and the ice to minimize the danger of gangrene.

General Diffuse Peritonitis.—The treatment here is identical with that of appendicitis. Should proctoclysis be adopted, it should be very gentle.

Gastric Diseases.—*Atony of Stomach.*—Brief cold applications, enhanced by kneading the abdomen, partially restore the lost tone and improve the sluggish circulation. The cold rub followed by a short cold hip bath may be used. The hot air bath or warm bath to induce visible sweating, by a jet or fan douche at 60° F., applied to the abdomen for ten to thirty seconds, is productive of benefit.

Acute Gastric Catarrh.—Hyperemesis yields, as a rule, to ice water or ice. The abdominal binder renewed every three or four hours may be employed. If high fever arises, general heat-reducing measures are indicated.

Chronic Gastritis.—If atony and dilatation of the stomach are associated with this disease they should be combated by the appropriate measures. The gastritis is treated by the half bath at 70° F., concluded by the pail-pour, repeated several times. Lavage often renders sturdy service in ridding the stomach of thick tenacious mucus. General invigorating treatment should be instituted. A cold rub upon arising, with subsequent vigorous mechanical stimulation and exercise, is followed by the jet and fan douche at 80° F. This temperature may be gradually lowered in the later applications, which should occur once every twenty-four hours. This treatment has proved very efficient.

Gastroptosis.—After a hot bath at 105° F. for five minutes, late in the forenoon, a spinal douche at 100°-102° F. of twenty pounds pressure is applied for ten seconds. Then the patient returns to bed, and the abdomen, particularly the epigastrium, is well covered by a hot wet flannel compress, which is heated by an electric pad and renewed two hourly. An elastic binder tightly encases all. This prescription is recommended by Lockwood.

Dilatation of the Stomach.—This morbid state is usually found in conjunction with atony, and its treatment is practically that of atony. Lavage of the intestines and irrigation possess special value in this disorder.

Nervous Dyspepsia.—The hot air bath at 160°-170° F. for six minutes, succeeded by a five-minute friction tub bath at 98° F.; then by the rain douche of twenty pounds pressure at 95° F., gradually lowered to 90° F.; and then by the spray douche at 80° F. for five seconds followed by mechanical stimulation, has given excellent results in the hands of Baruch. The jet and fan douches may be used with the temperature daily decreased.

Cold sitz baths at 50°-60° F., lasting from three to eight minutes; cold sheet rubs at 53°-64° F. upon arising, and brief cold shower baths are of service. The malady is very resistant to treatment.

Ulcer of the Stomach.—To promote a greater blood supply to the stomach is one of the initial remedial steps in treatment of ulcer. The cold sitz bath at 50°-54° F. for three to five minutes and trunk compresses combined with a brief application of the hot coil to the abdomen serve further to increase the blood flow. In addition, the last measure increases the alkalinity of the blood (Buxbaum). Cold compresses to the stomach are of service. To control hemorrhage one may place ice water or ice in the rectum and apply the cold stomach coil. The latter serves more efficiently when combined with the cold stomach compress. A strict dietary régime must be used in conjunction with the hydriatric measures.

As gastric ulcer frequently occurs in chlorotics, prophylactic treatment should be instituted in all cases of chlorosis. Cold sitz baths at 46°-57° F., for three to five minutes daily, abdominal packs renewed every three hours, with a fifteen-minute application of the abdominal coil at 104° F. once a day, are the measures often employed. A cold pack for twenty to thirty minutes, followed by half bath at 70° F. for two minutes, is of value. The pain is relieved by the application of the electric pad to the epigastrium.

Specific Infectious Diseases

While control of the body temperature is the cardinal aim of hydrotherapeutic measures in acute febrile disease, other manifestations of the toxemia should not be overlooked. The rapid heart, the lessened blood flow, the quickened shallow respiration, and the emesis are as cogent in their claims as the fever. The altered metabolism as indicated by the increase in the urinary ammonia, nitrogen, and the decrease in the urea nitrogen, the lessened alkalinity of the blood, and the alteration of the morphological elements of the circulatory fluids also claim attention. Hydriatric measures are able to exert a beneficial influence upon all these abnormal expressions. The applications in vogue are the partial ablution, the half bath, the full bath, the continuous bath, the hammock bath, the Brand bath, the wet pack, the cold rub, the trunk compress, and cold applications over the precordium and to the head.

Diphtheria.—The wet pack changed at uniform intervals, with the final application continued until visible perspiration appears, and then followed by a bath at 75°-82° F., combined with vigorous affusions, yields happy results. Ice finely subdivided applied in bags to the throat often modifies the disease.

Influenza.—Hot baths are recommended. Sheet baths may be effectual in increasing the systemic tone.

Exanthemata.—*Measles.*—Full baths at 103°-107° F., lasting from three to six minutes, according to the age of the child, given five or six

times daily, have met with wonderful success according to their sponsor, Dr. Grosse. As the disease is developing, baths at 95°-100° F. are frequently employed. Many merely sponge with cold water, especially if there be hyperpyrexia. Brief plunges into water at 55°-60° F. often influence the extreme cases. Pulmonary complications are considered later.

Scarlatina.—The remedial value of hydrotherapy in scarlet fever is manifest in the decreased death rate, the low percentage of complications, and the lessened period of infectivity of the disease. The applications may be either hot or cold. Warm or tepid sponging is applied twice daily in ordinary cases. The warm bath at 90°-98° F. given once in twenty-four hours is also effectual in cases of moderate severity. In desperate cases baths at 90° F., of five to ten minutes' duration, repeated every four hours, are very efficient in alleviating the symptoms. Hansom cites three characteristic cases in which these applications were of demonstrable value. The hot bath at 98°-104° F., or hot air bath, is employed to relieve anuria. Dry packs may be subsequently applied. Although a temperature of 103° F. is the indication for the application of cold, undue depression, tachycardia, and insomnia also demand it. The Kerley graduated cool pack, made of Turkish toweling, applied to the torso, and kept in place until the temperature is 102° F., is a valuable measure. The initial temperature is 90° F.; by reductions of five degrees every five minutes 80° F. is reached, at which figure the temperature is kept thirty minutes. At the expiration of that time, if the fever is not perceptibly diminished, the temperature of the pack is reduced to 70° F. or 60° F. Partial ablutions at 72°-80° F. of a duration dependent upon the readiness of the reactive response may be employed. In the early stages, affusions at 50°-70° F., following five to ten-minute full bath at 105° F., often relieve an embarrassed heart. The pyrexia may be reduced by graduated ablutions, which are instituted with a temperature of 90° F., and with each administration reduced one degree until 75° F. is reached. The wet pack may be employed. In a series of one hundred and ten cases treated by cool applications not one case of nephritis developed. Angina and adenitis are treated by cold compresses.

Syphilis.—Some increase in elimination of toxic materials is caused by the diaphoresis induced by the steam cabinet bath. Sweating may be also provoked by the dry pack. These processes offer no interference to the cutaneous absorption of mercury. On the contrary, they seem to enhance it. General stimulating measures are employed to increase the systemic vigor and offset the general effect of the circulating poison. Of these the cold shower bath following a one-hour application of the wet pack is quite effective. This procedure, however, should not extend over five days. The beneficial results obtained at such spas as Mt. Clemens and Hot Springs depend more upon the strict mercurial treatment ad-

ministered than upon the chemical properties of the various waters used in bathing. The value of the bath lies in the extreme cleansing of the epidermis which leads naturally to a more rapid and thorough absorption of the mercury. It is claimed that the waters of Aix-les-Bains, by the virtue of their calcium sulphid content, exert, when applied externally and internally, a partial curative effect in lues.

Tetanus.—The application of heat yields the better results, although cold measures have been the more employed. Of the warm applications the hot wet pack of 100° to 110° F. and the warm bath are most effective. Combined with antitetanic serum, they help to oppose the advance of the disease.

Pulmonary Tuberculosis.—Prophylactic treatment of tuberculosis affords a valuable field for the practice of hydrotherapy. The establishment of thorough prophylaxis is sometimes designated *"hardening."* It should be commenced early in those suspected of a tubercular predisposition. It is instituted by gradually lowering the morning bath to 86° F. The bath should seldom exceed ten minutes in duration, and when ended a cold affusion of 70° F. should be given, and then brisk friction applied. Older children may be immersed in water at 80° F. for one to four minutes, and rubbed vigorously while in the bath. Undue heat loss is avoided by making the application in the morning. Exposure to sunlight and artificial or natural sea bathing often serve to increase the general resistance.

When the disease has developed, cold sponging with ordinary tap water, practiced each morning, is valuable. Poor circulation is a contraindication to this procedure. The chest compress and the cross binder applied for long periods of time are useful remedial adjuncts in controlling pain, faulty respiration, expectoration, and cough. They also exert a favorable influence on the course of the disease, stimulating the encapsulation of infective foci and enhancing the absorption of caseous or necrotic tissue. This is probably due to increased pulmonary blood flow.

The Cornet method of hydriatric routine may be employed: The patient receives, at first, simple friction morning and night, until a strong reaction appears. After one week of this, friction is made with a cloth wet with water at a temperature of 92° F. This temperature is gradually decreased to 66° F. in the course of several treatments. One-half hour of rest is enforced at the end of the treatment. If this treatment has been tolerated well, two-minute rubs in a sheet wet with five per cent. salt solution, at 90° F., are inaugurated. The brine is made more cold each day until 60° F. is reached. An open air walk for one hour follows the treatment. Douches at 90° to 95° F. may be used, except when copious expectoration or increased nervous excitability is present. It is possible so to adapt patients to cold measures that they take douches

of tap water at a temperature of 40° F. during the winter, and apparently suffer no inconvenience. Another method consists in beginning ablutions at moderate temperature, 95° F., and gradually reducing the temperature daily, until 60° F. is reached. Then the ablution is supplanted by an affusion at 90° F., which in turn passes through the descending steps until 50° F. is obtained. The affusion is practiced daily. Four basins full of water are used at each treatment.

In the presence of fever all violent measures are contraindicated. The cool sponge bath usually controls the fever, but if it fails, ice rubs should be tried. Hemorrhage is met by ice bags or the cold Leiter coil to the thorax and the thighs.

Yellow Fever.—Diaphoresis by means of the blanket pack should be induced. In the beginning of the disease hot foot baths at 105°-110° F. may be tried.

Asiatic Cholera.—A cold rub in a sheet completely or partly wrung from water at 45°-50° F., or a half bath for two to five minutes at 68°-80° F., often prevents the appearance of diarrhea. Early enteroclysis with warm water often relieves the spasm of the intestine. A cold rub in a sheet at 32° F., followed by a sitz bath at 8°-12° F. for fifteen to thirty minutes, may check purging and favorably influence vomiting. Ice cooled water applied as rubs and sitz baths is indicated when the disease is very severe.

Cholera Infantum.—Cold baths are not advisable. The happiest results follow the use of baths 98°-100° F. given frequently for intervals of five to ten minutes. The addition of mustard to the bath will enhance the benefits accruing therefrom. Care must be taken, however, to protect the eyes from the irritation of the mustard and also from the infective agent of the disease. If convulsions appear or collapse or low temperature ensue, heat, either by the hot bath or incubator, or both combined, should be at once applied. The following methods taken from Budin-Maloney will prove of use to combat collapse, convulsions, and low temperature:

"Two methods of giving the hot bath may be followed. In one, the infant, having, let us say, a rectal temperature of 83.2° F., is plunged into water of 100.4° F. and left there fifteen to twenty minutes. The rectal temperature is then found to rise to progressively 95°, 96.8°, 98.6°, and 99.5° F. The infant is then taken out of the bath and placed in an incubator, and the rectal temperature taken several times to find the duration of the action of the hot water.

"In the other form of administration the infant is immersed suddenly in water which has a temperature one degree higher than that of the body, 95° F. in this case. The temperature of the water is then gently increased until it reaches 100.4° F. while the temperature of the infant gradually rises to 99.5° F. After twenty minutes it is placed in

an incubator. It is found that the temperature in the latter case remains nearer the normal, and falls slower than in the former."

Dysentery.—The form of this disease caused by amebic invasion of the intestine is treated successfully by cold enteroclysis with water at 40° F. or even ice-cold. The fluid should be administered gently in order to obviate pain. Ice suppositories may be tried in the bacillary variety. The careful introduction of warm saline solution into the colon after defecation is effective in controlling pain and diarrhea.

Typhoid Fever.—The best results of hydrotherapeutic management of enteric fever are obtained when the treatment is instituted at the onset of the disease. As a rule, the cold applications are employed, and of these the Brand bath enjoys most favor. While with some authorities it has been partly supplanted by less heroic measures, accumulated statistical evidence attests its efficiency. It is given as follows: A portable tub is placed by the bed and two-thirds filled with water at 70° F. An ounce of wine or a spoonful of alcohol is given twenty to thirty minutes before the bath, or four ounces of hot coffee may be administered just before immersion. After wetting the face with ice water, the patient is placed in the tub and the entire cutaneous surface mechanically stimulated by a sponge. The initial shock and the feeling of coldness usually incite desire in the patient to quit the bath, but in absence of symptoms of collapse or marked shivering, immersion should continue for fifteen minutes. Twice during the bath one-half gallon of water at 50° F. should be poured over the shoulders and head. A slow pulse of small volume does not indicate withdrawal from the bath. At the expiration of fifteen minutes the patient is wrapped in a sheet and blanket, placed on the bed, and, if his temperature exceeded 103.5° F., evaporation is permitted in order to increase heat loss. If shivering be extreme the skin is dried and he is returned at once to bed. Artificial heat is undesirable, but may be needed to insure reaction, although vigorous rubbing and curtailing the length of the next bath are superior methods of furthering the reactive powers. Four to six ounces of ice water are given twenty to thirty minutes after the bath, and an abdominal compress at 60° F., renewable hourly, is applied. The bath is repeated every three hours or oftener if indicated. A temperature exceeding 102.5° F., a low muttering delirium, extreme muscular twitching, insomnia, and other manifestations of toxemia demand immediate bathing. The total number of baths is variable; as many as one hundred and seventy-five have been given to one patient. The wonderful results of the Brand bath are shown by the fifty per cent. reduction of mortality from typhoid recorded by Dr. Thompson from New York hospitals. In Australia, of nineteen hundred and twenty-three cases so treated, only seven per cent. died (Hare).

Various modifications of the Brand bath have been offered. Affusions at 70° F., gradually lowered to 60° F., are endorsed by Cabot. The

hammock bath at 88° F., in which the patient is kept until the temperature taken per rectum is 100° F., whereupon the bath is omitted for two hours or until the temperature again mounts to 102.5° F., seems to be nearly as efficacious as the cold bath. The cold bath may be abbreviated from eight to five minutes and employed every three hours when a poor reaction results. As the recuperative powers increase, the duration of the bath is prolonged to fifteen minutes. The partial ablution is used also to test the reaction. The general effect of these modified baths is not equal to that of the original measure.

As mentioned above, some medical men regard the cold bath as too severe, and have devised substitutes entailing less distress to the patient. The ice rub, which is the strong application of a flat piece of ice to all of the body except head and neck, exposing only the part worked upon at a time, is warmly endorsed by Hare. A fall of two degrees in temperature and a slowing of the heart usually result from ice rubs; sponging with cool water is claimed to be effective in cases in which the temperature is not over 101°-102° F. The graduated bath beginning at 95° F. and closing at 80° F. is employed. Full warm baths at 88° F. shortened the course of the disease and reduced the mortality from ten to eight and one-half per cent., according to Riess, who has employed this measure in eight hundred and nine cases. A temperature of 102° F. requires the tub for five to ten hours until the rectal temperature is 100° F. It seems, however, the substitutes fail to equal in efficacy the Brand bath. The statistics concerning these modifications are incomplete, but yet they indicate a higher death rate than follows the use of the Brand method.

Hemorrhage is met by rest and cold abdominal applications. Ice may be used with due precautions against gangrene.

Malaria.—All applications should anticipate the paroxysm, for once the chill begins it cannot be checked. Abortive treatment is efficient. A cold douche at 60° F. under twenty to thirty pounds pressure to the back for five minutes, with a simultaneous hot foot bath, has proved a valuable routine prescription. Cold hip baths and cold douches have cured malaria of several years' standing after arsenic and quinin had failed. Two hundred and seventy-two reported cases have yielded to hydrotherapy alone. The following prescription is effective: A hot air bath is given for five to ten minutes about one hour before the chill. Then a douche or affusion at 60° F. is applied over the spine, spleen, and liver from thirty seconds to a minute. The douche should be used at a pressure of from twenty to thirty pounds. While the douche is applied a hot foot bath at 100° F. should be given. These may be prescribed again in one-half an hour and two applications preceding the chill are usually able to prevent its appearance. Should a seizure appear a wet pack at 65° F. is useful in reducing the temperature and promoting elimination.

Cerebrospinal Meningitis.—Cold applications, such as the ice bag or Leiter coil, to the head and back of the neck are indicated. Hot baths at 104° F. for twenty to forty minutes, repeated four times daily, lessen the pain, spasm, and tenderness and may modify the disease. Early commencement of the treatment is of prime importance. In one series of fifty-one cases treated by hot baths the death rate was thirty-three per cent. The hammock bath at 93°-100° F. may be tried. The following routine is the method of applying the hot bath: The patient enters a cushioned bath at 90°-93° F., which is then slowly raised to 104° F. After twenty to forty minutes have elapsed he is lifted out by means of a sheet, if much pain be present, and then covered by a blanket. This procedure is also applicable to the meningismus of children. If tenderness be extreme the patient should always be moved bodily on a sheet. As a result of the bath the tenderness diminishes, the temperature falls, the restlessness and spasm decrease, and the patient sleeps.

Pneumonia.—Cold applications are selected to treat pneumonia. These may be the ice bag, the cold Leiter coil, the Brand bath, half bath. The ice bag and coil are placed on the chest and on the head. The reduction of the toxemia with strengthening of the heart's action and of the vessel tone is the desired aim of the treatment. The beneficial results of cold hydriatric treatment are illustrated by a death rate of about three per cent. in the report of five hundred cases managed by cold applications. Chest compresses and cross binders are valued measures. Alcohol given before and after a bath often averts cardiac weakness. The treatment for adults is the Brand bath, the details of which were discussed under typhoid fever. The chest compresses wet with ice water and renewed when dry or warm, or even every ten to twenty minutes, are valuable measures. The half bath at 65°-72° F., of five minutes' duration, coupled with vigorous rubbing and affusions at 50° F., is also effective. The ice bag should be applied over gauze to the thorax and base of head. An abundance of plain water should be administered, by mouth, if possible. A hot mustard foot bath under blankets, to which hot water is continuously added, maintained for forty minutes, is valuable for the diaphoresis it induces. In the aged, adipose, and intemperate the heart must be given careful attention.

In children the cool wet pack and sponging give excellent results. Compresses from 75° to 80° F., enveloping the child from the base of the neck to the navel, are also used.

Diseases of the Nervous System

Cerebral Anemia.—This may be either a symptom of organic change in the brain or a manifestation of morbid processes elsewhere. In either case the underlying disorder should be determined and should be met

with the appropriate treatment. The anemia may be combated by profuse sprinkling of the face and chest with cold water at 75° F.

Cerebral Hemorrhage.—The application of an ice bag or cap or the cold Leiter coil to the head, combined with the compresses to the trunk, are the customary hydrotherapeutic measures in treatment of hemorrhage of the brain.

Cerebral Hyperemia.—As this condition usually manifests itself by marked sleeplessness, measures which afford relief for insomnia may be effective in lessening the cerebral blood supply. Douche applications to the spine, coupled with strong friction, and cold measures to the head and the wet pack applied from thirty minutes to one hour are the means usually selected to secure the desired effect.

Chorea.—In event of heart complications the precordial coil should be applied. Full baths at a temperature from 90° to 98° F., and not allowed to fall below 80° F., during the bath of one hour's duration, should be given once daily. At the conclusion of the bath the extremities are gently kneaded. Wet packs applied from one to one and one-half hours in conjunction with the precordial coil exert a decided calmative effect. The coil should be applied intermittently at thirty-minute intervals. A half bath of 86° F. for five to ten minutes should follow the application of the wet packs. A few treatments have effected complete cure in some cases.

Epilepsy.—Hydrotherapeutic measures exert a twofold effect in the treatment of epilepsy. They hinder the progress of the disease and reinforce the action of drugs. Thus, with the aid of hydrotherapy, convulsions may be averted or lessened in severity by smaller doses of bromids and the unpleasant condition known as bromism may be avoided. Half baths at a temperature from 80° to 86° F., lasting from eight to fifteen minutes, and sitz baths at 85° F., show valuable effects. The baths may be followed by affusions and intense rubbing. In the young and robust, baths of 75° F., gradually lowered to 68° F., and of a few minutes' duration, are recommended by Binswanger. Hydriatric measures are ineffectual to check a seizure once established.

Headache.—Headache is often caused, or accompanied, by cortical hyperemia, so the diversion of the blood flow from the brain and the cord to the superficial vessels is indicated. This may be accomplished by the hot foot bath in water at 95° to 100° F., lasting ten minutes. A cold foot bath, 45° to 50° F., of two minutes' duration, followed by strong friction, is equally as potent. Cold compresses changed hourly should be applied to the head. The cephalalgia so frequently a symptom of brain neoplasm may often be lessened by hot mustard foot baths and hot compresses applied to the spine.

Hemicrania.—This obstinate malady sometimes yields to wet packs applied from one to one and one-half hours and followed by cold rubs. The

drip sheet is recommended. Mechanical manipulation and friction, preceded by diaphoresis induced by the hot air bath or any general measure, may be useful.

Hysteria.—The treatment is mainly symptomatic. Pain and increased sensitivity yield to long-continued cold applications. The cold compress of 65° F. may be used. The cold jet douche with an initial temperature of 80° F., gradually decreased to 40° F., applied for one minute, is very effective in diminishing sensory excitability. Anesthesia usually yields to the same applications. An ice rub is often an excellent remedy.

The cold Leiter coil to the spine most admirably controls extravagant motor activities, such as cough, respiratory spasm, and hiccough. A cold water spray of 50° F. or a brief cold douche at the same temperature allays the respiratory excitement, while the troublesome hiccough is arrested by the application of an abdominal binder in conjunction with a hot abdominal coil. Contractures, if recent, often are alleviated and removed by the use of the hot coil or full hot baths to 104° to 110° F.; if long established, wet packs continued for one to two hours may be tried. Muscular atrophy is best combated by mechanical kneading. If paralyses exist, brief cold measures are indicated to improve the errant innervation. The cold rub at 60° F., the cold half bath at 65° F., and cold brief shower baths should be employed.

The following prescription is useful in the treatment of hysteria, particularly when associated with marked despondency: The hot air bath is applied for five minutes; then the circular douche, under twenty-five pounds pressure, at 85° F., and reduced gradually to 60° F., is administered for thirty seconds. The spray douche at 65° F. is then given for five seconds, and finally the jet douche at 50° F. is applied for three seconds over the back. This treatment may need to be prolonged for months.

Insomnia.—Sleeplessness is frequently associated with cerebral hyperemia, but even if it depends upon other factors a derivative vascular action is highly desirable. The wet pack for one to one and one-half hours is an admirable measure. Nightly sitz baths at 80° F., lowered two degrees every day, until 50° F. is reached, applied for three minutes, are of value. The warm bath at 90° to 98° F. applied for thirty minutes before retiring may produce sleep if the patient, after being rapidly dried, be hurried into a warm bed. The room must be warm and there must be no delay between emergence from the bath and entrance into bed. When insomnia is due to a relative ischemia of the feet the best treatment is a running cold foot bath for a few minutes, followed by drying with a rough towel (Broadbent). A cold wet towel applied around the neck while a patient is in bed may yield sleep. Sea bathing often has a soporific effect.

Acute Myelitis.—The application of the cold coil to the spine for a

long period of time gives the best results. The temperature should be kept at 54° F. When the acute process has dwindled, half baths and the hammock or continuous bath may be employed. Heat should never be used in the early stages of the disease.

Chronic Myelitis.—The hammock bath at 95° to 100° F. and the continuous bath under the same thermic conditions, may exert a beneficial effect. The half bath at a temperature of 82° to 86° F. given from four to eight minutes with moderate friction and gently applied affusions should be tried.

Neuralgia.—Warm baths are of benefit to the neuralgias of the head. The hot fomentation may be tried. In sciatica the Scotch douche achieves wonderful results. The steam cabinet or the hot bath pack followed by the cool half bath may be substituted for the Scotch douche. The latter exerts its greatest effects in recently developed cases. Indeed, one treatment may cure. The effect of the jet and of the Scotch douche, following a warm application, is decidedly happy. A hot air bath at 175° F. for eight minutes, followed by a jet douche applied to the spine and the affected part for thirty to sixty seconds, beginning at 90° F. and decreasing to 60° F., may be employed. Then under twenty-pound pressure the Scotch douche at 60° and 105° F. is directed against the vertebral column. Ice bags to the sciatic nerve have been endorsed. The antineuralgic value of hydriatric measures is demonstrated by the record of Winternitz's clinic. He treated five hundred and eighty-five cases of all types of neuralgias, and all but twenty-nine were cured or improved.

Neurasthenia.—A "neurovascular training" as devised by Baruch is an absolute necessity to the majority of neurasthenics. Great care must be practiced both in the reduction of temperature and in the change of measures. To commence, an ablution of 85° F. may be given every morning and daily the temperature be lowered until an ablution of the trunk with very cold water is succeeded promptly by a good reaction. Then the ablutions are supplanted by affusions, which are graduated in the same fashion. Later the drip sheets supersede the affusion. The fan douche at 80° F. is then applied for one minute to the trunk and the extremities and is followed by the jet douche at 70° F. on the back for thirty seconds. The temperature of both douches is decreased one to two degrees daily until the lowest tolerable degree of cold is reached, while the pressure is slowly increased to twenty pounds. Half baths at 78° to 86° F., coupled with affusion and rubbing until a good reaction results, are of value. Later, cold applications may follow. To avoid heat loss the treatment should be given upon arising or after the hot wet pack or hot air bath. The salt rub with subsequent fan douche at 92° to 99° F. applied from four to eight minutes along the spine, thorax, and extremities possesses great value.

Neuritis.—The hot applications usually afford great relief. The hot bath pack, hot compresses, and hot baths of 104° F. may be used. The steam douche is valuable for its derivative action. Should the neuritis arise from trauma an ice pack or a poultice should be employed locally. Magnesium sulphate compresses at 50° F. may be used for the neuritis due to alcoholism. Wet packs applied one hour daily hasten recovery after tenderness subsides. An affusion at 50° to 60° F. should follow the pack.

Occupation Neuroses.—Shower baths at 45° to 60° F., combined with a fan douche at the same temperature, applied locally, yield excellent results. The cold coil, ice poultice, and the ice bag as continuous measures are valuable auxiliaries. The ice bag and ice poultice should be withdrawn fifteen minutes in each hour. Low temperature applications are aided by strong mechanical stimulation. Passive motion is highly effective.

Paralysis.—Toxemias and intoxications are responsible for many of the limited palsies; in these cases the general emunctories should be stimulated. Circulation to the paralyzed parts should be increased. The steam bath or the hot air bath for eight to fifteen minutes, succeeded by a cold ablution at 45° to 55° F., or a cold rub, produces excellent results. The Scotch douche and the wet pack at 65° F. for two hours are useful measures. The palsies which follow diphtheria are benefited by the daily use of half baths at 70° to 75° F. for two to five minutes. Vigorous affusion should accompany these baths.

Tabes Dorsalis.—Happy results are often produced by alternating temperature applications followed by gentle rubbing. The thermic range of these applications should be very slight. Baths at 95° to 100° F. for thirty minutes to one hour may be employed. For the arterial spasms, irrespective of the site, alternating temperature sitz baths and the cold coil placed to the spine may be tried. As a rule, however, the crises are little affected by treatment. The following prescription from Hinsdale is effective in the beginning of the disease: The hot air baths for eight to ten minutes, the circular douche under twenty pounds pressure for two minutes at 90° to 105° F., followed by the jet douche at fifteen pounds at 85°-100° F. for one minute. Then for one-half minute at 85°-105° F. under fifteen pounds pressure the Scotch douche is applied; and the fan douche at 80°-85° F. under fifteen to twenty pounds pressure for twenty seconds, followed by an alcohol rub, concludes the treatment. Daily the temperature should be decreased and the pressure increased until the fan douche reaches 70° F. and Scotch and jet douches are driven by a force of twenty pounds. Half baths at 80°-85° F. applied from five to ten minutes may be used in the late ataxic stage. If the ataxia is marked or paralysis is present circular douches at 100° to 105° F. under twenty pounds pressure, applied for one minute, following the ap-

plication of the hot air bath for ten minutes, are of value. The fan douche at 105° F. to 120° F. will increase the effect. Moderate sea bathing may be of value, but should be employed very cautiously. The hammock bath at 100° to 105° F. is of benefit.

Spasmodic Tic.—Cold shower baths at 40° to 55° F. for one to two minutes produce the best results in this disorder. In general, stimulating measures are applied, but the treatment is unsatisfactory.

Mania.—In cases of cerebral excitement which accompanies alcoholism, dementia precox, chorea, epilepsy, paresis, puerperal states, and general acute manias, the hammock bath produces excellent results. The temperature of the bath should be between 95° to 100° F. and should never fall below 95° F. Covering the top of the bath tub with a blanket or other covering prevents heat radiation and tends to keep the temperature of the water constant. When the bath is continued for several hours reduction of the excitement is produced. The duration of the bath, if the patient gives no contraindications, is proportionate to the amount of excitement present. When the bath is ended the patient should be quickly covered by a warm blanket and rapidly placed in a warmed bed. Daily douches graduated from 100° to 75° F. decrease the cerebral exaltation. The continuous bath applied daily from ten to twelve hours at a temperature from 95° to 105° F. gives even superior results to those obtained by the use of the hammock bath. Profuse diaphoresis induced by means of hot air, electric light, or steam cabinets succeeded by a rain bath of five minutes at a temperature of 95° F., decreased to 80° F., is of value.

Diseases of the Joints

Rheumatoid Arthritis.—Hydrotherapeutic efforts are directed toward the mitigation of pain, the promotion of mobility, and the improvement of circulation. Five-minute applications of the hot air bath (165° F.-175° F.) followed by rapid ablutions of water of an initial temperature of 95° F., and reduced one degree each day until 60° F. is reached, often yield valuable results. The circular douche at a temperature above 85° F. is a useful auxiliary measure. Additional means are the circular compresses and the Scotch douche.

Arthritis Deformans.—Hot water baths are contraindicated except in the earliest stage of the disease. Hot air baths, hot sand baths, and electric light baths exert most potent effect in checking its progress. It is possible by these means to reduce the amount of inflammatory fluid in and around the joints, and to increase the range of movement of the articulation, if extensive hyperplasia of the joints be not present. The circular jet and Scotch douche applied for a length of time, depending upon the individual case, should follow these applications of heat.

Gonorrheal Arthritis.—In the acute stage the moist heat of hot baths and hot douches at a temperature of 100° to 105° F., is indicated. Hot dry packs for one hour should follow these measures. Local applications of hot compresses will often ameliorate the pain in very severe cases, in which there should be no massage of the affected parts. In chronic gonorrheal arthritis douches are extremely potent measures. They are best applied after a hot air cabinet bath of from five to fifteen minutes' duration. The jet douche at twenty pounds pressure is usually employed as a test measure, and if it is well tolerated it is continued with gradually increased pressure up to thirty pounds. In the more chronic cases full pressure cold douche, and moderate manipulations are the measures of choice. A careful watch must be kept for the usual cardiac accompaniments of an acute arthritis.

Acute Articular Rheumatism.—In those who possess the so-called rheumatic tendencies prophylactic hydrotherapeutic measures may avert the development of the disease. Moderately cold salt water baths at 85 to 90° F., with subsequent marked rubbing for ten to fifteen minutes, often rectify the rheumatic predisposition. In the treatment of the actual disease, if the pulse exceeds 90 and great tenderness be present, baths in the tub are contraindicated. With a pulse at eighty, tub baths of an initial temperature of 98° F. may be used. If endocarditis or pericarditis be present, the temperature should not exceed 98° F. at any time. The cold precordial coil applied for thirty minutes to one hour, two or three times a day strengthens the heart and may prevent the occurrence of cardiac complications. The temperature may be reduced and elimination increased by the repeated use of the wet pack. Two or three are given, and the last is maintained in place until diaphoresis occurs. Then a bath at 95° to 100° F. of five minutes' duration is given. In absence of much pain the pyrexia may be lowered further by a cold rub after the concluding wet pack is removed. An increase in fever and pain warrants a repetition of the complete procedure. Milder cases may be treated by sponge baths at 104° to 110° F., three minutes, with succeeding friction in cold water at 60° and 70° F. If hyperpyrexia (105° to 106° F.) be present, the following routine will yield excellent results: The patient is placed in a bath at a temperature of 85° to 95° F., which is then slowly reduced to 60° F. The duration of the bath is from fifteen to thirty minutes, being concluded when the fever drops to 101° F. If the temperature descend even to 98.5° F., after withdrawal from the bath, in the absence of other signs, no alarm need be felt.

Local magnesium sulphate compresses at 140° to 160° F. if changed constantly may exert a marked amelioration after the procedure has been in force twenty minutes. Water at 70° F. is applied with rubbing, after which rest in bed is required for at least an hour. Even during con-

valescence a cold rub should be given upon awakening in order to lessen the danger of relapse.

Intoxications and Toxemias

Alcoholism.—*Acute Alcoholism.*—The relief of this condition obtained by the use of the Turkish bath is a matter of lay knowledge. A prolonged warm bath at 100°-102° F., with subsequent inactivity, preferably in bed, may be substituted for the Turkish bath.

Chronic Alcoholism.—Saline infusion may be given for nervous manifestations, such as excitement, insomnia, and neuritis. They often yield to prolonged wet packs. Many cases respond best to hot tub baths, lasting five to twenty minutes, at 102°-104° F., with subsequent hot pack for ten to twenty minutes. In absence of vascular disease cold sponging may be employed.

Chronic Arsenic Poisoning.—Elimination of the offending agent is the hydrotherapeutic aim. Steam cabinet baths lasting ten to fifteen minutes, and the hot air cabinet, for the same length of time, followed by Scotch and jet douches or a cold rain bath, are efficient in this respect. Wet packs often exert an analgesic effect upon the intense pain sometimes present in arsenical intoxication.

Chronic Mercurialism.—The use of the hot tub bath at 104° F. for ten to thirty minutes with the succeeding use of hot dry blanket packs for twenty minutes is advocated. An alcohol rub is usually given when the pack is discontinued.

Chronic Morphinism.—The treatment of this habit is similar to that outlined for chronic alcoholism. General invigorating procedures are valuable.

Chronic Plumbism.—Elimination by all channels should be increased. The means at our disposal to accomplish this is the steam cabinet for fifteen to twenty minutes or the hot air cabinet bath. Douches, as the circular or fan, should follow these diaphoretic measures. Colic may be relieved and elimination from the intestine aided, by enteroclysis. Three to five liters of warm water may be used, and, if expulsion ensues, may be repeated in one-half hour. The hot abdominal coil has also proved of service in controlling colic. Paralytic conditions are treated by Scotch douches and cold fan douches.

Chronic Nicotinism.—Here the treatment may be conducted as in chronic alcoholism.

Thermic Fever.—Treatment should be instituted without delay. Cold measures, combined with friction, are indicated, but some relief can be accomplished by simply hurling cold water against the body. Ice cold sprays and affusions, cold sheet rubs with vigorous friction, ice cold enemas, and ice rubs are the measures usually adopted. The ice pack is pernicious.

Irrespective of the form of treatment used, the patient should be completely disrobed and frequently renewed ice pads should be placed to the neck and an ice cap adjusted to the head.

When the temperature is high, 106°-110° F., a cold sheet bath accompanied by strong rubbing should be continued until the temperature reaches 102°-103° F. During the bath the patient should have cold water thrown over him, and after the bath should be placed in bed with the ice cap in position. Enemas gradually reduced from 90°-45° F. should be given in amounts from four to five pints. These may be given until the axillary temperature falls to 102° F.

The O'Dwyer treatment with affusions had the best results in the New York epidemic in 1896. The mortality with this form of management was only six per cent., while with all other forms it ranged from eleven to thirty-three per cent. This treatment is as follows: After the patient has been covered by a sheet and placed on a stretcher, an attendant standing a few feet away from the patient hurls cold water from a dipper on him until the temperature taken per rectum is 103° F. As the body cools vigorous friction is given.

The cold sponge bath is of value. The flower-pot ice water spray may be used.

BALNEOLOGY

Introduction

Balneology is concerned with the treatment of disease by mineral waters. A mineral water is a water from a natural source, which contains mineral substances in solution. Since no natural water is absolutely free from minerals, all waters found in nature may be classed as mineral waters. There is, therefore, no sharp distinction between balneology and hydrotherapy. Hydrotherapy deals mainly with the external application of common water; balneology with the external and internal application of waters from special sources.

The therapeutic actions inherent in special waters not by virtue of the aqueous nature alone, but by virtue of the potency of the dissolved constituents, are utilized in balneology. At some springs only drinking is employed; at others mainly bathing; but at most both bathing and drinking are practiced. Vichy waters have specific curative properties in diabetes and glycosuria; earthy waters cure gravel and stone; Creuznach is especially efficacious in uterine complaints; Aix-la-Chapelle in syphilis. Chemists have elaborately analyzed these waters to detect the elusive property in which the remedial power resides. Weary columns of statistics reveal even the most minute traces of organic or inorganic, solid or gaseous matter which the water contains, but cast no light upon

the mode of action of the waters. Springs which contain the most diverse mineral substances in the proportions which are most dissimilar enjoy apparently an equal potency in the treatment of the same disease. Different persons with the same disease may not be curable at the same spring. Artificially prepared waters of apparently identical composition are admittedly less efficacious, and even questionably useful.

To what, then, does the natural source owe its value? Recently radioactivity has been demonstrated in the waters of many springs. Doubtless such radioactivity is powerful to benefit; but the patient must first be thoroughly educated to its significance and then be convinced of its presence. To the less credulous the waters have properties more tangible and commonplace. If analysis shows a special source to be well aerated and to contain sodium, calcium, or other base combined with hydrochloric, sulphuric, or other acid, the merit of the water is that inherent in water the world over, plus that due to its gaseous, metallic, or metalloid constituents. The value of such constituents is their essential value. It is no mysterious virtue. Iron or arsenic exerts the same pharmacological effect whether it be administered as a natural solution or as a pharmaceutical preparation. The action of alkaline or of sulphuretted waters does not vary when it is sought in an Arcadian spa and when it is invoked in a crowded town. The worth of balneological treatment lies not in the water and its contents. These have a certain importance, but the prime factors in the cure are the psychic influences which accompany it; the absence of work and worry; the change of climate and environment which invest it with healthy interest; the regulation of sleep and diet and exercise which reinforce it; and the medical skill which controls all.

In spas, to every mental stimulus of a non-religious nature which tends to health, appeal is made. The physician who recommends the treatment begins the therapeutic suggestion by his declaration of faith in the spa and his panegyric on the evidences of its curative powers. A belief in the efficacy of the spa is accepted by natives as part of their national inheritance, one of the virtues of their fatherland; by foreigners, as conferring upon them at once a certain exclusive cosmopolitanism. The pinnacle of faith is reached by the spa doctor who sees in the waters a cure for everything, from fibroid tumors to supernumerary digits. At the spa itself everybody assembles for one purpose—to strive for health. The social instinct among the similarly sick, the atmosphere of salutary competition among convalescents, the regular restful hygienic mode of life pursued, and the climatic conditions enjoyed, exercise a cumulative curative action on the overstrained, the depressed, and the weary. Dietetic and hygienic regulations are more or less stringently enforced. The régime in itself is curative for the majority of the slightly ailing who flock to these resorts. The routine flushing of the system with innocuous

fluids eliminates the lingering toxins of years. In nearly all spas the medical skill at the disposal of the visitors is excellent—skill in handling the particular maladies which are specially catered for at the spa; and, particularly, skill in alleviating slight conditions superimposed upon the main disease, conditions which can be remedied by attention to therapeutic detail. The health resort physician takes cognizance of every mental and physical aspect of his patients. His psychotherapeutic skill is, as a rule, far superior to that of his colleague in general practice. Aided by the atmosphere which pervades such places, an atmosphere similar to that which Bernheim helped to create at Nancy, and supported by municipal and institutional authority, the doctor of the spa is in the position of a health-giver whose word is law. His rule is salutary. His prescriptions are edicts of health which all must obey. No private physician could impose such a régime, could practice such beneficent tyranny, as is welcomed at spas. Spas are little more than institutions where hygiene, hydrotherapy, and faith healing are practiced, and often the greatest of these is faith healing.

Composition of Mineral Waters

The mineral waters contain either saline or gaseous constituents, or both. They are used internally and externally. Externally they are used as baths partly on account of the stimulating action of their contained salts and gases, and partly on account of the elevated temperature which they often have.

The mineral constituents of spa waters are derived from the percolation of rain water through the soil and through various strata of the earth's surface. On analysis of them, sodium, potassium, magnesium, calcium, iron, manganese, lithium, and arsenic are the usual bases encountered; they are combined with hydrochloric, sulphuric, carbonic, hydrobromic, and hydriodic acids. Silica is often present. Sometimes the metals occur as sulphids. Oxygen, carbon dioxid, nitrogen, sulphuretted hydrogen, and other gases may be present in solution. These gases may be present under considerable pressure. Often the gaseous tension is such that the water is bright and sparkling, and on exposure to atmospheric pressure effervesces.

Temperature

The temperature of the waters varies greatly. Waters which issue hot, derive their heat from that which exists at great depths in the earth. Indeed, it has been alleged that the hotter the spring the deeper is its source. At Virginia Hot Springs the temperature of the water ranges from 110° F. to 78° F.; at Arkansas Hot Springs, from 93° F. to

150° F.; at Salt Lake Hot (Sulphur) Springs (Utah), from 110° F. to 128° F.; at Aix-la-Chapelle (Germany) it is 167° F.; at Carlsbad, 162.5° F.; and at Bath (England), 120° F.

Classification

The amounts of the various constituents vary greatly in different sources. According to the essential constituents of the water, sources are classified as indifferent, alkaline, saline, chalybeate, sulphurous, etc. Many waters do not belong to any one group. Thus, saline sulphur springs are common; others could rightfully be classed in any of several categories. Hence, this mode of classification does not distinctly differentiate, but merely groups somewhat similar waters conveniently together. The following are some of the most important sources:

Simple Thermal Waters

Simple Thermal Waters include waters of high temperature and small mineral content.

America.—Virginia Hot Springs; Berkley Warm Springs; Warm and Hot Springs, Buncombe Co., North Carolina.

Great Britain.—Bath; Buxton; Matlock.

France.—Bagnères de Bigorre; Néris; Bagnoles de l'Orne; Plombières; Dax; St. Amand.

Germany and Austria.—Badenweiler; Teplitz, Bohemia; Gastein, Salzburg, Austria; Wildbad, Wurtemberg; Schlangenbad (near Wiesbaden).

Italy.—Battaglia; Bormio; Pozzuoli.

Switzerland.—Loeche-les-Bains; Ragatz.

These waters are usually "soft"; they are not frequently used internally, but are employed almost solely as baths.

Common Salt Waters

As common salt is of almost invariable occurrence in natural waters, this class has indefinite and arbitrary limits. In the waters comprised here common salt is the essential constituent.

America.—Fruit Port, Michigan; Grand Haven, Michigan; Mount Clemens Mineral Springs; Spring Lake Well; Salt Spring, Virginia; Ocean Spring, Alabama.

Great Britain.—Droitwich (brine, 300 parts per 1,000), Worcestershire; Nantwich (brine); Woodhall Spa (chloro-bromo-iodid), Lincolnshire.

France.—Bourbonne-les-Bains (hot); Salies de Béarn; Chatelguyon

(warm, gaseous); Salins du Jura; La Mouillière (chloro-bromo-iodid); Salins Moutiers (warm).

Germany and Austria.—Baden Baden (weak, 2 parts per 1,000); Nauheim (warm, gaseous); Hesse (near Frankfort-on-Main); Berchtesgaden, upper Bavaria; Oeynhausen, Westphalia; Homburg (cold; contain also bicarbonate of iron) (near Frankfort-on-Main); Ischl, Salzkammergut, Austria; Reichenhall, Bavaria; Kissingen, Bavaria; Soden (near Frankfort-on-Main); Kreuznach, Rhine Province; Wiesbaden (hot).

Switzerland.—Bex; Wildegg.

Alkaline Waters

Waters containing sodium bicarbonate. Three subgroups: 1, Simple alkaline waters; 2, alkaline and common salt waters; 3, alkaline and sodium sulphate waters.

America.—Capon Springs, Virginia; Glenwood Springs, Colorado; Glen Summit Springs, Pennsylvania; Geyser Spa, California; Gettysburg Springs, Pennsylvania; Manitou Soda Spring, Colorado; Minnequa Springs, Pennsylvania.

France.—Vals, 1;* Vichy, 1; Allier; Royat, 2.

Germany and Austria.—Bilin, 1; Fachingen, 1; Carlsbad, 3, Bohemia; Neuenahr, 1, Coblentz; Franzensbad, 3, Bohemia; Ems, 2, Hesse Nassau; Marienbad, 3, Bohemia.

Switzerland.—Tarasp, 3.

Bitter Waters

These contain chiefly magnesium sulphate:

Great Britain.—Cheltenham (chlorids also); Leamington (chlorids also).

France.—Brides.

Germany and Austria.—Apenta; Friedrichshall; Pullna.

Spain.—Rubinat.

Chalybeate or Iron Waters

These waters contain iron in medicinal quantities:

America.—Rawley Springs; Rock Iron Springs; Church Hill Alum Springs, and others, Virginia; Sharon Springs, New York; Pacific Congress Springs, California.

England.—Tunbridge Wells.

France.—Forges-les-Eaux; Orezza.

* The figures refer to the subgroup.

Belgium.—Spa.

Germany and Austria.—Bocklet; Pyrmont, Waldeck; Bruckenau; Rippoldsau; Elster, Saxony; Schwalbach; Petersthal.

Italy.—Santa Catarina.

Switzerland.—St. Moritz.

Calcaréous Group

These waters contain salts of alkaline earths, calcium and magnesium sulphate, and carbonate:

America.—Cherry Valley, New York; Holston, Virginia; Chittenango, New York; Waukesha, Wisconsin; Clifton Springs, New York; Tate Epsom, Tennessee; Bedford, Pennsylvania; Alum Rock, California; Catoosa, Georgia, etc.

England.—Bath.

France.—Bagnères de Bigorre; Contrexéville; Vittel.

Germany and Austria.—Inselsbad; Lippspring; Wildingen.

Switzerland.—Loeche-les-Bains; Weissenberg.

Sulphur Waters

These waters contain sulphids. Many of them also contain chlorids. Some of them are warm:

America.—Calistoga Springs, California; Santa Barbara Springs, California; Glenwood Springs, Colorado; Hot Sulphur Springs, Colorado; also in Utah and Arkansas.

British Isles.—Ballynahinch (Co. Down, Ireland); Harrogate, England (13 per 1,000 NaCl); Dandrindod Wells, Wales; Moffat, Scotland; Strathpepper, Scotland.

France.—Aix-les-Bains (warm); Louchon; Allevard; Pierrefonds; Amélie-les-Bains (hot); St. Honoré-les-Bains; Barège; St. Sauveur; Canterets (warm); Uriage; Eaux Bonnes (warm).

Germany and Austria.—Aix-la-Chapelle; Baden; Weilbach, Nassau.

Switzerland.—Baden; Heustrich; Schinznach; Gurnigel; Lenk.

Egypt.—Helouan.

Arsenical Waters

These waters contain arsenites or arsenates.

America.—Crockett Arsenic Lithia Springs (Virginia); Thompson's Bromine Arsenic, North Carolina; Harbin Hot Sulphur Springs, California.

France.—La Bourboule; Boussang; Vals.

Germany and Austria.—Cudowa; Roncegno; Linda Pausa; Levico, South Tyrol.

Italy.—Civilina; Ceresole Reale.

The Action of Mineral Waters

The effect of the ingestion of the large quantities of water which forms part of the routine treatment at Mineral Springs is to flush out the stomach, intestine, kidneys, and other organs. The water, by its bulk, stimulates peristalsis and voids in solution or suspension, the putrescent material from the bowels. Some of the water is absorbed. The bulk of the circulating fluid is increased; the greater volume affords endocardial stimulation and the circulatory efficiency may be enhanced. The resulting increased blood pressure promotes diuresis. The vital processes are all quickened; tissue change increases; mucous membranes secrete more freely; and the skin glands function more actively. To dilute toxins; to dissolve them; and to promote their excretion, are the main actions of water.

But a feeble atonic stomach musculature may not lightly tolerate the ingestion of large volumes of water; embarrassed hearts may perceptibly fail under the added burden which must be propelled; and overworked diseased kidneys may quickly be exhausted by the laborious functional activity thus demanded.

Action of Salines.—The dialytic and irritant properties of salines inhibit absorption of liquids, augment peristalsis, and increase the fluid contents of the intestines, so as to produce more or less free purgation. The presence of increase of salts in the blood causes a livelier interchange between the circulating blood and the fluid in the tissue spaces; diuresis ensues; a mild expectorant action is produced; and metabolism generally is increased.

Salines are said to increase the solubility and diffusibility of albumins. In food a considerable amount of salt is customarily ingested. How far the added quantities of salines, which are absorbed during mineral water cures, exert an influence on metabolism, is doubtful. The action of the salines varies somewhat according as the base and the acid radical which they contain. The action of the metallic element need not further be discussed here. The rate of diffusion of chlorids, sulphates, and iodids determines whether they are essentially purgative or diuretic. Radicals of large molecular weight, such as sulphates, with difficulty diffuse and, therefore, tend to act mainly as cathartics. Whereas, with radicals of small molecular weight, such as chlorids, an interchange takes place readily between the bowel contents and the portal circulation, so that a considerable proportion of the salt may be ingested. Further details as regards the mechanism of the action of salines belong more properly to the

realm of pharmacology. Salt and bitter springs are used in constipation, portal stagnation, chronic gastroenteritis, chronic respiratory, pelvic, and rheumatic conditions.

Alkalies.—The alkaline waters increase the alkalinity of the blood plasma, promote tissue changes, increase metabolism, and tend also to increase the alkalinity of the urine. As alkalinity promotes the action of the saliva, bile, pancreatic, and intestinal juices, alkalies enhance digestion. Alkalies are alleged to facilitate respiration (Voit) not only in the tissues, but also in the lungs, by acting as carbonic acid carriers. The alkaline waters are used in acid dyspepsia, constipation, gall stones, gravel, gout, glycosuria, and obesity.

Iron, Arsenical, Sulphid, and Earthy Waters.—Waters containing iron and arsenic in sufficient amounts to be of therapeutic value exert merely the ordinary pharmacological action of these substances. They are used mainly in anemias, neuralgias, and skin diseases. The action of the sulphid waters is not evident. They are said to stimulate secretion of bile and to have an expectorant action. Their use in syphilis is greatly lauded, but where it is most exalted, mercury is also given as a substantial prop to its curative powers. Sulphids in sufficient quantity are protoplasmic poisons. To class the sulphid mineral water as an alterative is to admit ignorance of the basis of its action. The earthy waters, those containing the sulphates and carbonates of calcium chiefly, have probably little action apart from that of the water. They are given as antacids, as astringents, and sedatives, in acid dyspepsia and in diarrhea. Their benign flushing power is used in hepatic and gouty conditions, and in chronic cystitis, gravel and stone.

Resultant Action of Mineral Waters.—Few waters have only one content. As the waters were classed according to their predominant constituent, so is their action regarded as being that mainly of this essential constituent; but the predominant constituent of any mineral water is not that which occurs in greatest quantity, but that which is most active medicinally. Some waters containing small quantities of arsenic exert more action by virtue of their arsenic than they do by virtue of all their other constituents. We therefore have to deal with compound actions, some of which are negligible, and some of which are important. Of the important actions some reinforce and some tend to neutralize those of the other constituents. The precise effect therefore of any given mineral water is the resultant of so many actions that it is difficult to presage, and we must more or less empirically base our expectations of its value upon observations of physicians and patients.

In addition to these mineral factors the presence of carbonic acid gas also modifies the action of the waters. The carbonic acid is supposed to be at once stimulating and sedative. It certainly renders waters more pleasing to regard and more palatable to take.

Many mineral sources yield waters at high temperatures and the temperature effect also modifies the therapeutic action.

Indications for, and Choice of, a Spa

In considering the indications for these waters we must not too strictly view their pharmacological characters. Many springs of totally different composition cure the same diseases, and springs of analogous composition are lauded for efficacy in dissimilar maladies. There is, in addition to the actual effect of the waters, the result of the change of climate, of the improved hygienic conditions, of the absence from mental stress, and of the completely novel environment. In many cases change of air alone will prove efficacious. The treatment consists mainly of change, not of betterment of climate. This is especially evident in anemia. An anemic country girl visits a town and is benefited thereby; an anemic town girl returns rosy from the country. Whether the town girl goes to the sea, or the moors, or the mountains, the change has the same beneficent effect. Hence, in dealing with blood conditions, balneological treatment is usually unnecessary. A happy result may be obtained merely by change of scene and air. Now, all these factors, the complex pharmacological actions of the waters, the spa psychotherapy, the change of climate, the regulation of the mode of life, are common to most spas and tend to deprive any one resort of valid claim to essential properties not possessed by any other. The choice of a spa for any given case is thus rendered a matter largely of experiment. It ought to be regarded as an experiment, so that if, after adequate time, the patient does not satisfactorily improve, another spa may be tried. Instead, now, of entering into an analysis of the virtues of the different spas for different diseases, or of the indications which would induce a physician to determine between several similar spas in any given case, we shall briefly deal with a few of the more important diseases and mention merely the general factors which influence one's choice of a spa for the treatment of these diseases.

First, the desirability of balneological treatment and the patient's ability to bear the cost, the journey, the change, and the treatment must be determined. Unless balneology promises markedly better results than would accrue from pharmaceutical treatment; and unless the patient's pecuniary and physical state warrant the recommendation, then the suggestion of a spa should not be made. Once having determined that a spa is desirable the physician considers accessibility of the spa, its climate as regards temperature, wind, and moisture, its elevation above the sea level, the accommodation which it provides, the nature of the waters, the bathing, massaging, and exercising facilities, and above all the quality of the medical skill available. These considerations determine his choice. In weakly patients a preliminary course of treatment may be necessary at

home before any journey is attempted. Thus, in severe heart cases, a modified Nauheim treatment may first be instituted by the private physician; then a home spa may be utilized in order to strengthen the patient for the long, rough journey, or the stormy sea voyage, or the rigors of the new climate, and then the possibly more desirable and efficacious foreign spa is attempted.

Climate of Spa.—As regards the climate, raw, damp, cold regions would naturally be contraindicated in acute pulmonary conditions or in convalescence from pneumonia. High altitudes, while dry and rare and calm, afford greater variations of temperature and are not desirable for the sleepless and mentally distressed, nor should they be visited by severe heart cases, arteriosclerotics, apoplectics, and those with a tendency to hemoptysis. Then, convalescents from acute diseases, also, had better not be sent to mountainous health resorts. For all these the sea level is better, for the sea climate is more equable.

The Spa Itself.—The chemical composition of the water is not a matter of great moment. More important are the bathing facilities, the provision for physicotherapy, and the housing arrangements. Unless good food and good accommodation are insured the spa should be avoided. For the slightly ill the social life of the spa is an important therapeutic factor. But the most essential point of all in the choice of a spa is a knowledge of the medical skill available. A spa, where a local physician is personally known to the physician who sends the case should, if possible, be selected. Just as a physician would not readily recommend his patient to a surgeon for whom he could not personally vouch, so should he be chary of committing his case to the care of an unknown health-resort physician. Arrangements for the patient should be made before the journey is commenced, so that when the invalid arrives at the spa all unnecessary discomfort and delay may be avoided. With the patient a full account of his malady and its treatment should be sent. Much must be left to the discretion of the local physician at the health resort, but the family physician should know whatever is proposed for the treatment of the patient he sends, why it is proposed, and what it promises. Home spas should always be recommended whenever possible. The season at most spas is from May 1st till September 30. Many, however, especially those with thermal springs, are winter resorts also.

Tardy Convalescence

A patient convalescing is in a state of physical and mental instability and has so little reserve strength that fatiguing journeys must be avoided. All spas which practice heroic methods are emphatically contraindicated. No "flushing" treatment to exhaust the heart and to fatigue the kidneys should be considered. A change of air alone may be all that is necessary.

If a spa be selected it should be one in which the treatment is gentle and not fatiguing—a mild, near, warm, sheltered spa, at a low altitude. If the patient is markedly anemic a spa with iron waters or with iron and salt waters should be chosen. In convalescence from special diseases some spas are said to be particularly efficacious. Kreutznach, Woodhall, and Kissingen are lauded in convalescence from inflammatory pelvic conditions. In these spas remains of inflammatory exudates, chronic endometritis, perimetritis, and salpingitis are said to disappear; even fibroids are alleged to melt under the solvent action of these waters. After rheumatic fever, when the joints remain painful, and the heart dilated, Nauheim or Rheme may be advocated. For the neuralgia, which so often follows influenza, malaria, and other affections, Schlangenbad is highly recommended.

Special Balneology

Diseases of the Blood

Anemia.—It is essential, first, to consider whether the patient be suffering from primary or secondary anemia. In the primary anemia of adolescents constipation is so often a causative factor that good results are frequently obtained by the use of the mild aperient waters of any of the saline or thermal springs. Such waters alone may effect a cure. But before, during, and after the spa treatment pharmaceutical preparations of iron may be exhibited. If a mixed salt and iron spring be available the treatment may be begun there and then finished at another spring containing more iron. Often climatic change alone suffices to effect a cure, and no change is more generally useful than that which is obtainable by a sea voyage. In the anemia which follows repeated losses of blood from hemorrhoids, the mildly purgative springs, which tend to reduce portal congestion, are indicated. In the anemia due to chronic renal conditions, great care is necessary: the diseased kidneys are already overstrained; the demand made upon them by the ingestion of a great volume of fluid may complete their undoing. In the anemia of incipient tuberculosis, especially that complicated by hemoptysis, a warm, sheltered, low altitude spa is desirable. In the anemia of syphilis, sulphur springs, such as Aix-la-Chapelle, are recommended. In all anemias it is essential, first, to recognize the underlying cause and then to choose the spa suited to the treatment of the primary disease.

Diseases of the Respiratory Organs

The main respiratory diseases seeking balneological treatment are chronic bronchitis and emphysema, asthma, and tuberculosis. Persistent

traces of exudate after pneumonia are also often subjected to spa treatment. The essence of the treatment, so far as the respiratory tract is concerned, is to improve the climatic conditions. Bronchitis and emphysema arise from many causes—respiratory, renal, cardiac, vascular, etc. The cardiac and vascular, and perhaps the renal case, may be benefited by appropriate waters. The slight expectorant action of the alkaline and saline waters may also directly help the relief of the morbid process in the lungs. For the tuberculous patients rest, feeding, sun and light, and fresh-air baths are necessary.

Cardiac Diseases

With cardiac cases careful consideration is imperative before a visit to a spa be attempted. In severe valvular conditions the patient is better at home. Long journeys and bulky water treatment are more liable to kill than to cure. If spa treatment be contemplated in such cases a preliminary course of Nauheim baths (see Chronic Myocardial Insufficiency) should be given at home. The heart muscle should also be strengthened by cardiac tonics such as strophanthus or digitalis. Even when the valvular disease or the myocardial change be not severe the journey should not be rashly undertaken, and it is desirable to travel by short stages.

A beginning should be made with rest after the journey. Then Nauheim baths of short duration and about body temperature should be given. Gradually the baths may be cooled and lengthened. Then the carbonic acid gas may be added to them. Finally, the Schott exercises may be attempted. Later, the Oertl treatment, regulated walking, and the climbing of slopes, may be practiced when the heart has been strengthened enough to allow of its use.

The hearts most benefited by spa treatment are the weak, fat, flabby hearts of overindulgence in everything except exercise. [The special indication for Nauheim treatment is chronic myocardial insufficiency of the first and second degree, it should never be employed in the third stage. (See Chronic Myocardial Insufficiency.)—EDITOR.] The dietetic and hygienic régime and the graduated work often act as a charm in such cases. If the heart is weak, graduated exercises are very cautiously initiated. Passive movement alone is first attempted; next, active movements; then resistance movements; and, finally, the Oertl exercises. In the dilated fatty heart of anemia the cause of the anemia should be the chief object of treatment. The guiding principle should be "to hasten slowly." Excessive work may damage a dilated heart so as to require months of treatment to remedy the indiscretion. Very little good comes from the ingestion of water: and positive harm may accrue if the water be aerated.

Renal and Bladder Diseases

Since the work of Von Noorden and his school the popularity of balneological treatment in kidney diseases has rapidly waned. It is now generally admitted that to fatigue the kidneys by imposing upon their already feeble energies the labor of excreting large quantities of fluid, is of very doubtful therapeutic wisdom.

The cause of gravel lies in dietetic errors. No treatment should be instituted before the precise chemical composition of the urinary deposit is determined. Then rational dietetic measures are the best means to combat the tendency. To render the urine alkaline by ingestion of alkaline waters in bulk, is to precipitate the urinary phosphates and to add a phosphatic layer to the calcareous nucleus already present. The flushing of the urinary system with waters containing small amounts of calcium carbonate and phosphate—the so-called earthy waters—is in itself harmless and of little efficacy. Equally good results could be obtained by drinking quantities of warm water on an empty stomach at home. As the cause of calculus formation is usually disease of the bladder wall, local medicinal treatment of proven value must not be neglected for the more ornamental but less useful bath treatment.

Rheumatism

No one would think of moving a case of acute rheumatism to any Spa, however praiseworthy. In the prolonged convalescence which follows sometimes, in cases which persistently relapse slightly, which continue to have tender, painful joints, which show slight valvular or myocardial changes, or which are pronouncedly anemic, a change to a spa often works wonders. When joint changes are the main impediment to health, when thickening and effusion persist, a spa should be chosen with alkaline or sulphurated saline waters, a hot spa, a spa in which Zander exercises, massage, and good bathing facilities are obtainable, so that absorption of the morbid products may be hastened. When cardiac trouble is the residue then Nauheim or some other spa, where cardiac troubles are specially treated, should be selected. The anemic cases should be sent to an iron saline spring. The climate of the spa selected should be equable, warm, and dry. Most of the good results of spa treatment in rheumatism can with care and skill be obtained from physicotherapeutics at home.

Alimentary Disorders

It is among the indiscreet of habit, the people who work too much and eat too little, and those who eat too much and work too little, that the benefits of spa treatment are most pronounced. In the dyspeptic, the

gouty, the "livery," the spas find their most grateful patients. The myriad of minor ailments of alimentary origin, and of importance in direct proportion to the neurotic and to the financial disposition of the patient, yield to the dietetic regulation of the spa. The purgative waters clear the channels of life from accumulations of ages. Constipation is not permitted; the portal circulation is stimulated to activity; hepatic congestion disappears, and piles and pelvic disorders are mitigated or banished. The gouty concretions are dissolved; the system is flushed clean; contributory dietetic errors are rectified; and the high specific gravity of the urate-loaded urine is lowered.

Much work requires yet to be done before we can have a satisfactory rational basis for the treatment of the lesser ailments. Experience and experiment guide us to send patients with atonic dyspepsia to sources with hypertonic waters; to send acid dyspeptics to the mildly alkaline saline springs; and to send the obese and the gouty to the sources of strong waters, such as Carlsbad and Marienbad. After treatment with drastic catharsis, prolonged rest and judicious feeding are necessary. If these cannot be obtained then less heroic measures should be used and springs such as Contrexéville employed. Or even milder measures may be quite as efficacious, and a course at Buxton or Bath suffice.

After all spa treatment a rest in a bracing climate for several weeks is strongly to be advocated before the patient recommences the routine of life.

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CHAPTER V

THE PRINCIPLES OF MEDICAL CLIMATOLOGY

Henry Sewall

Definition and Scope of the Subject.—As pointed out by K. E. Ranke (37) and by R. DeC. Ward (44), the words Climate and Climatology have various significations according to the point of view from which their content is regarded.

The word *climate* is derived from the Greek κλιμα, which means an inclination or slope; it indicated the supposed slope of the earth's surface from equator to the poles. The idea must thus have included distinctions in the length of the day, heat and cold, and distribution of the forms of life. In its physical aspects, climate is determined by the facts of meteorology, or science of the atmosphere; and this in turn is inseparable from physiography, which pertains to the structure of the earth, and the distribution of its various features. According to Hann (17), "By climate we mean the sum total of the meteorological phenomena that characterize the average condition of the atmosphere at any one place on the earth's surface. That which we call weather is only one phase in the succession of phenomena whose complete cycle, recurring with greater or less uniformity, every year, constitutes the climate of any locality. *Climate* is the sum total of the *weather,* as usually experienced during a longer or shorter period of time at any given season."

But in ordinary usage the word *climate* inevitably suggests a relation between the physical conditions of earth, air, and water to be found in any place, and the sensations and activities of man.

The vital relations of the physical elements of climate are well illustrated in the distribution of the various forms of animal and plant life. Man himself, through his ability to make fire and clothing and to command food, has been able to adapt himself to the widest extremes of climatic conditions.

When a plant or an animal flourishes in a given locality, its organs and functions are said to be adapted to the conditions there found. To a great extent such forms, or their descendants, may be brought, by gradual change, to live in a totally different environment.

This adaptability of living beings to widely different external conditions, through which forces which were once destructive become again conservative of life, depends upon a *physiological reaction* of the living organism to the influences acting on it. The physiological reaction of protoplasm to internal and external agencies determines the nature, the distribution, and the evolution of all forms of life.

As we view the races of men in their habitats, from the poles to the equator, it is obvious that the differences between them are more or less dependent upon adjustment to their various environments. This adjustment involves not only the externals of clothing, the struggle for food, and the general habits of life, but strikes into social and moral relations, and results in anatomical differences, at least of form and color. What may be called *physiological climatology* seeks to determine what are the vital reactions especially evoked in various climates; what functions of the body are specifically stimulated or soothed; and what may be the effect, on the organism as a whole, of any definite climate. Human history is still too brief to enable us to certify whether limitations of physiological adaptation rigidly restrict the geographical distribution of a given race of men without fundamental change in their ethnographic characters. Caucasian peoples are rapidly claiming the whole earth, and it is a matter of urgent moment to learn the natural adaptations they must acquire to best conserve their preëminence under new conditions.

Until recently the problem of physiologic adaptation to climate has been inextricably confused with the incidental effects on man of the climatic distribution of pathogenic microorganisms. While the white man has acquired a certain degree of immunity against the infections common to temperate zones, he is so susceptible to the disease-provoking organisms teeming in the tropics that no fair opportunity has been allowed for his normal development in such regions. The migrations of the white race have been limited by the geographical distribution of pathogenic protozoa, and of certain insects which serve as their intermediate hosts.

The extraordinary demonstration in Cuba, the Philippines, and the Canal Zone, that the infections which had threatened the lives of strangers in those regions are rigidly under control of Sanitary Art, for the first time gives the immigrant opportunity to adjust himself to tropical conditions. Enough has already been learned through the health reports from such localities to make it probable that morbidity and mortality among healthy adults, at least, are not essentially increased or accelerated by residence in tropical climates. As Clemow (9) says: "Many—almost the majority—of the ordinary infective fevers are most prevalent in the cool, and not the warm, season of the year." In temperate climates the transmission of the most important infections depends more or less upon the intimacy of contact between the sick and the well; and the applica-

tion of hygiene involves a regulation of sociologic relations. Reference will be made later to the modification of physiological functions under tropical conditions.

While these views of climatology have a broad bearing on ethnogeny and eugenics, the human interest in the subject to-day is especially concerned with the influence of climate upon the sick man; or as an environment antagonizing the inception of disease. As the welfare of the human being in his conflict with disease, whether this is infectious or constitutional, depends, in general, on physiological reactions which lead to the development of compensations, adaptations, or antidotes within the organism, it is obvious that the study of *medical,* no less than *physiological, climatology* has to do with vital reactions to climatic conditions.

The first step in such a study should afford a comprehensive view of the physical elements of climate and the results of their combinations in actual climates. Then should follow an account of observations and experiments upon the physiological reactions of normal beings to the physical conditions of climate, singly and combined. Finally, consideration should be given to the natural distribution of diseases and to the effect of climates and climatic factors in conserving or antagonizing the forces of the human organism in its struggle with disease. It is obvious that the scope of medical climatology must automatically shrink with the development of specific therapeutics and preventive medicine.

METEOROLOGICAL CLIMATOLOGY

The Factors of Climate.—Climates owe their characters to the quantitative relations of certain physical elements, the principal of which are: (1) temperature; (2) atmospheric moisture or humidity; (3) atmospheric movements or winds; (4) soil; (5) water; (6) electricity. As will shortly be seen, various other relations are of salient importance. These are: latitude; the geographical distribution of land and water; ocean currents; the existence of mountain chains and elevation above the sea; insolation, and atmospheric composition, including impurities.

It is obvious that the various factors of climate may have a very different relative importance, according as they are viewed as agents affecting the physical conditions of the earth, or the welfare of forms of life upon it. The biologic importance, for example, of direct insolation and of winds probably far outweighs the physical influence of these factors.

TEMPERATURE.—From all points of view, probably the most important single factor of climate is *temperature.* With the sun vertical over the equator, a beam of energy which covers a unit area of the earth would

be distributed over a progressively larger surface if deflected obliquely toward the poles. It is said that the amount of solar energy falling upon a given area along any meridian at midday varies approximately as the cosine of the latitude. Less heat, therefore, descends upon a given area of the earth with increasing obliquity of the rays. Moreover, as the shell of atmosphere enveloping the earth has, especially through its watery content, considerable power of absorbing heat, it is obvious that oblique rays, which pursue a longer atmospheric path, are correspondingly robbed of their heating power. Three conditions determine the insolation, or amount of solar energy, received at any place:

(1) The obliquity of the rays, according to which less heat falls upon a given surface; obliquity increases with latitude.

(2) The relative length of day and night. The ratio of day to night increases with latitude, in summer. As pointed out by W. L. Moore (29), in his recent admirable work, "The rapidly increasing length of the day toward the poles during summer soon more than compensates for the decreasing angle at which the solar rays strike the earth"; so that during summer the insolation is actually more abundant at the poles than at the equator.

(3) The absorption of solar energy by the air. In dust-free air the absorption of heat depends upon the presence of contained watery vapor and carbon dioxid. With increasing obliquity of the rays more air is traversed and more heat absorbed. Watery vapor and carbon dioxid have a specific absorptive power for the longer rays of the spectrum.

The following table copied from Moore's work represents the intensity of insolation at different solar altitudes:

INTENSITY OF INSOLATION AT DIFFERENT SOLAR ALTITUDES

Altitude of the Sun	Relative Length of the Path of Rays through the Atmosphere	Intensity of Insolation on a Surface Perpendicular to the Rays	Intensity of Insolation on a Horizontal Surface
0°	44.70	0.00	0.00
5	10.80	0.15	0.01
10	5.70	0.31	0.05
20	2.92	0.51	0.17
30	2.00	0.62	0.31
40	1.56	0.68	0.44
50	1.31	0.72	0.55
60	1.15	0.75	0.65
70	1.06	0.76	0.72
80	1.02	0.77	0.76
90	1.00	0.78	0.78

Although the earth is actually nearer to the sun in the winter of the northern hemisphere than in the summer, the greater relative obliquity of the rays during the former season is the chief cause of its cold. In the southern hemisphere, on the contrary, summer occurs in perihelion and winter in aphelion. We should, therefore, expect to find a much greater difference between the extremes of annual temperature south than north of the equator. Meteorological observation shows that such is not the case; the northern hemisphere has a climate of extremes, while the southern hemisphere has a relatively equable climate. The explanation lies in the fact that the land of the globe is chiefly aggregated in the former and the water in the latter. This brings us to the consideration of the climatic relations of *land and water.*

The specific heat of water is about four times that of land; that is, the same amount of solar energy would raise the temperature of a given body of land four times as high as that of an equal weight of water. Land is generally a poor reflector, but readily absorbs the heat falling upon it, and as readily gives it back to the air by radiation. Land is also a poor conductor, so that the heat absorbed is retained near the surface. Water reflects a considerable proportion of the incident heat. Water is a fairly good conductor, and the heat absorbed penetrates somewhat deeply and is evenly distributed. Heat reflected from the surface, or in evaporating the fluid, takes no part in warming the water.

The difference in density induced by the equatorial heat and the arctic cold, respectively, leads to the establishment of a convection circulation in the water, of which the great ocean currents are the most striking manifestations. The warmed water of equatorial zones moves along the surface toward the poles, whence deep reverse currents sweep to the equator to be warmed in turn. The Gulf Stream of the North Atlantic is generally credited with maintaining the temperature of the British Isles and northwest Europe far above that normal to the latitude. This effect is largely due to prevailing warm winds which blow from the sea. The influence of such air movement is to a great extent determined by the height of the coast line or the existence of mountain ranges parallel to it. Most littorals, and consequently to a greater or less degree the inland surfaces, have their temperature modified from that normal to their latitude by the contiguity of either warm or cold ocean currents. The important consideration in this place is the general fact that large bodies of water oppose extremes and tend to conserve a uniform temperature.

By the temperature of a place is meant the temperature of the air above it. This depends primarily upon the sun's rays, but may be much modified by reflection or radiation of heat from neighboring surfaces. A sleeping room at night may be uncomfortably warm from the radiation of heat absorbed during the day, although the air without is cool. The streets of a city under the summer's sun have, by reason of reflection and

radiation of heat, a much higher temperature than is normal to the air. An overcast sky reflects the heat radiated from the earth and at night prevents the normal cooling of the air. Farmers protect delicate plants from frost by suspending over them a sheet which reflects the heat radiated from the ground. In fact, the conditions of temperature and moisture near the surface are apt to differ widely from those found at even slight elevations in the free air. The variations near the surface are extreme and rapid, and depend upon the physical properties of the soil and its covering. If there is no wind, a thin stratum of cold air may stay in contact with the ground, but warm air would rise by convection. Therefore, meteorological observatories are elevated above the accidental influences of the surface.

The true air temperature can only be obtained from a thermometer placed in the shade and removed from proximity to reflecting and radiating surfaces. The temperature due to direct insolation, such as affects a person standing in the open, is measured by a special thermometer having a blackened bulb inclosed in a vacuum, and which is suspended in the sun. The lowest temperature of the day is registered shortly before sunrise, while the highest comes an hour or two after noon. Similarly, the warmest period of the year is about a month later than the summer solstice, and the coldest period follows the winter solstice after about the same interval. The mean temperature of the twenty-four hours is obtained by adding the figures of several observations, as those made at 7 a. m., 2 p. m., and 8 p. m., and dividing the result by the number of readings. It is obvious that two places may have the same mean temperature, while in one the diurnal temperature range is very great, and in the other very small; a matter of great physiological importance. A true estimate of the temperature changes of a place can only be obtained through records which show daily, monthly, and yearly means, as well as means of maximal and minimal temperatures for the same periods. The temperature relations of different places throughout the globe may be graphically portrayed and understood at a glance by the construction of *isotherms*. These are lines joining various stations having the same temperature (in general the mean temperature) at the same time.

The isotherms of high southern latitudes, where there is relatively little land, run nearly parallel to the equator throughout the year. But in the northern hemisphere, containing the great continents, the isotherms in summer reach higher and in winter lower over the land than over the water. That is, once more, under the same variations of insolation, continental temperature changes are sudden and extreme, while oceanic temperature changes are gradual and moderate.

Atmospheric Humidity.—Humidity denotes the moisture contained in the air. When the water is in the form of gas it is said to be diathermanous. But collected in the form of droplets, even if visible as clouds,

it has great capacity for absorbing heat. Hence, in murky or cloudy weather, the changes of air temperature are less extreme than when it is clear. Temperature and humidity are almost inseparable in their climatologic and physiologic relations. The atmosphere always contains more or less watery vapor. The amount of vapor which it can contain without condensation into liquid particles increases with the temperature. A definite weight of water when evaporated will saturate a definite cubic space at a definite temperature. The amount of vapor thus sustained is nearly indifferent to the gases already present. If the temperature of a saturated space be lowered, part of the vapor will be condensed. If the temperature rises, more vapor can be sustained. The following table (36) represents the maximal quantity of water that can exist as vapor in a cubic foot of space at various temperatures:

Temperature	Number of grains of aqueous vapor in a cubic foot	Temperature	Number of grains of aqueous vapor in a cubic foot
100° F............	19.8	30° F............	1.9
90° F............	14.8	20° F............	1.2
80° F............	10.9	10° F............	0.8
70° F............	8.0	0° F............	0.5
60° F............	5.7	-10° F............	0.3
50° F............	4.1	-20° F............	0.2
40° F............	2.8		

The actual amount of vapor contained in a given volume determines the *absolute humidity*. This, as just seen, has a maximum which increases with the temperature. The ratio of the amount of vapor actually present to that necessary to saturate the space at a given temperature is known as the *relative humidity*.

Thus, if it requires 10 grains of vapor to saturate a cubic foot of air at a given temperature, and but 7 grains are actually present, the relative humidity is 70 per cent. The amount of vapor remaining the same, the relative humidity falls as the temperature rises, and *vice versa*. These relations gain their importance from the fact that the rate and amount of evaporation from a surface depend largely upon the capacity of the air for absorbing moisture.

The lower the relative humidity the more powerful is the evaporating force. A knowledge of the absolute humidity of the air is sufficient for the purposes of the physicist, but the relative humidity expresses conditions of more physiological importance. Air at high temperatures can be "very dry," and still contain more moisture than cool air, which is "very damp."

The atmospheric humidity is determined by the *psychrometer,* which consists of a pair of thermometers, the bulb of one of which is covered with muslin moistened with water. The mercury of the "wet bulb" instrument stands at a lower level than that of the "dry bulb" to an extent determined by the rate of evaporation from the moist muslin. The readings of the wet bulb are thought to represent the "sensible" or physiological temperatures more nearly than those of the dry bulb. The action of wind greatly accelerates evaporation; a low degree of humidity which might be comfortable in the still air of a room would be disagreeable in the moving air of the open. Some observers prefer to consider not the relative humidity, but its complement, the "saturation deficit," which is the percentage of vapor which the air lacks for its saturation. The drying power of the air is determined by the percentage of watery vapor which is needed to saturate it. Thus at 30° C. (86° F.), with relative humidity 80 per cent., the amount of water that can still be taken up is about the same as when the air temperature is 10° C. (50° F.), and its relative humidity is only 36 per cent.

In changing from the liquid to the gaseous form, water absorbs a great amount of heat, rendering it latent and insensible to the thermometer. This heat of vaporization is taken from the air and especially the surface, from which evaporation occurs. When the vapor is condensed by falling temperature, its latent heat is returned to the air, and the cooling by that extent is checked. The "dew point" is the temperature at which vapor is condensed upon surfaces chilled by radiation below the saturation temperature of the air.

The absolute humidity of any region depends, in general, upon the extent of water surface, including the moisture of vegetation, exposed to evaporation. It varies but slowly from time to time. The relative humidity, on the other hand, rises and falls rapidly, inversely with the temperature. It is higher in the morning than in the afternoon. The capacity of the air to hold moisture rises with the temperature. The rate of evaporation decreases with the rise of relative humidity, but increases with the temperature of the moist surface and especially with wind movement which removes the humid layer of air in contact with it. Evaporation is increased in high altitudes, both because of the lowered barometric pressure, and by reason of the low per cent. of moisture in the air (17). As the amount of water which the air can hold depends upon the temperature of the latter, and as the temperature rapidly diminishes with altitude, it follows that most of the vapor is confined to the lower layers of the atmosphere. About half the watery vapor lies below the level of 6,500 feet, and nine-tenths below 21,300 feet of altitude (Hann). The intricate and profound relations of heat and moisture to physiological functions will be dwelt upon in a subsequent section.

Rain is due to the condensation of the vapor of the atmosphere when

it is chilled to the dew point. The tiny droplets thus formed coalesce to a greater or less extent before they fall. Solid particles suspended in the air under ordinary conditions serve as condensation centers for the rain drops. It is said that in saturated, dust-free air condensation may begin on suspended ions.

Rain washes and purifies the air and becomes of great hygienic importance to the atmospheres of large cities. Rain is more abundant in warm than in cold countries; and in regions where large surfaces of water are exposed to evaporation, provided the conditions for sudden chilling in the upper air are present, as on windward shores and in hill districts. Moisture-laden air, on striking a range of mountains, is deflected upward, and, being cooled, is apt to precipitate its moisture as rain on the windward side.

WINDS.—The chief cause of wind is an unequal heating of the air. Air expands or contracts by 1/491 of its volume for every degree F. of rising or falling temperature. Warm air is specifically lighter than cold air, and when masses of air at different temperatures are contiguous, they move down or up with velocities determined by the difference of densities. The foundation of wind on temperature is simple in explanation, but fundamental in importance.

A patch of sandy soil gets hotter under the sun than a surrounding surface of clay. The superior radiation from the sand heats the air just above it, and the heated air rises as if in a chimney, the cooler surrounding air continually pressing in and replacing it at the surface, to be warmed in turn. The column of expanded air, on reaching a greater or less height, flows over upon the surrounding bed of cooler atmosphere. Wind is the movement necessary to the restoration of equilibrium of density throughout the atmosphere. As aqueous vapor is specifically lighter than either oxygen or nitrogen, a given volume of moist air is lighter than that of dry air at the same pressure and temperature. Humidity is, therefore, a cause of winds. Winds are classified as permanent, periodic, and non-periodic. "To the permanent winds belong the trade winds, the antitrades, and the prevailing westerlies of high latitudes; to the periodic winds belong monsoons, land and sea breezes, mountain and valley breezes; to the non-periodic winds belong the high winds that accompany cyclones and anticyclones, including the hurricane of the West Indies, the typhoon of the China Seas, the simoom of Arabia and Africa, the sirocco of Italy, the föhn winds of the Alps, the chinook winds of the northwestern part of the United States, the mistral of Europe, the Texas northers, the blizzards, and the hot winds of our western plains, tornadoes, the thunderstorm gusts, whirlwinds, and many others" (29). In this article only the general features of the subjects can be discussed.

Warmed air rises as it expands, and cooled air descends as it con-

tracts. The contrast between currents of different temperatures is particularly obvious where they are confined, as among the slopes and valleys of a mountainous region. Uniform terrestrial wind movements largely depend upon the heating of the air in equatorial regions. A vertical motion is thus given to the medium and the air, being heaped up in the higher altitudes, flows off north and south to about latitude 30°, where, having become denser than the supporting medium, it descends to a greater or less extent in a vertical direction. Air currents on the surface of the earth have, of course, the reverse direction to those above. The dense air of the polar circles flows equatorward until it meets the surface currents moving poleward, when it ascends vertically, to be distributed again according to the relative densities. As Phillips (36) puts it: "The final result would be surface winds on the equatorial sides of latitude 30° toward the equator, and on the polar sides toward the poles; surface winds within the polar circles toward the equator; regions of variable winds and calms at the equator, latitude 30°, and the polar circles. The circulation, however, would still be along meridians." These ideal relations are somewhat changed by the axial rotation of the earth. As the actual velocity of rotation on a meridian increases from pole to equator, a mass of air moving southward is, in the northern hemisphere, left behind its appropriate meridian and becomes directed southwest. The result of this motion is seen in a deflection of meridianal currents, so that in the northern hemisphere north winds become northeast, and south winds become southwest in direction. In the southern hemisphere the deflections would be complementary.

The so-called *trade winds* of lower middle latitudes have their explanation in such rotational deflections of meridianal currents. Such relations hold well over the oceans, but the modification of temperature conditions over continental areas, and especially the obstructive and cooling influence of mountain ranges, complicate the actual wind movements.

The orderly connection between temperature and wind is familiar in the daily land and sea breezes on the coast line of any large body of water. The specific heat of land and water being about as 1 to 4, the land is rapidly heated in the day time, and the air expanding above it flows seaward in the upper regions. The cooler air over the water takes the reverse direction along the surface, thus giving rise to the tempering sea breeze of a summer's day. At night the land rapidly loses heat by radiation, and the air above it becomes more condensed than that above the water. The result is a nocturnal land breeze which lasts until temperature equilibrium is again reached.

Cyclones and Anticyclones.—During summer the excessive heating of continental areas leads to the generation of upward air currents many hundreds of miles in diameter. The lowest barometric pressure under such an expanse of upward motion is about at its center. The denser

surrounding atmosphere flows in from all directions along the surface toward the point of lowest pressure. The actual direction of wind movement, however, is not radial toward the "low" center, but, following the law of meridianal motions, the currents in the northern hemisphere take a circular direction opposite to that of the hands of a watch. Such a system of wind movement is known in meteorology as a *cyclone*. Conversely, when a column of air becomes heavier than the atmosphere in general, as commonly happens over continents in winter, the denser air moves vertically downward and passes outward along the surface from this center of high barometric pressure. For obvious reasons, the direction of wind motion in such a case is, in the northern hemisphere, like that of the hands of a watch. Such a system of wind movement is known as an *anticyclone*. The physiological effect of the cold, dry, pure air thus brought to the surface is one of invigoration. The reader is referred again to the comprehensive work of Moore for a graphic account of the meteorological bearings of this subject. Winds are of very great importance in medical climatology. They may furnish in turn the most grateful relief from the depressing effects of heat and moisture, or render an otherwise enjoyable climate unbearably rigorous.

Altitude.—The factors of climate are more or less modified with elevation above sea level. The weight of the atmosphere and, therefore, the barometric pressure decrease progressively in a vertical direction from the surface of the earth. When the barometer reading at sea level is 29.97 inches Hg, at an elevation of 5,000 feet it is about 24.97 inches, and at 10,000 feet 20.39 inches. The rate of fall decreases progressively. In the first 1,000 feet of elevation the pressure is lowered by 1.15 inches Hg, in the tenth 1,000 feet by only 0.77 inch Hg. According to Boyle's law, the volume of a gas varies inversely with the pressure, the temperature remaining the same. Therefore, the atmosphere is progressively rarefied with increasing altitude; the proportion of its constituents remains the same. At an elevation of about 3.5 miles, or 18,480 feet, the pressure is reduced to about half that of sea level. Permanent human habitations occur at altitudes approximating this (over 16,000 feet in Thibet and Bolivia—Hann). As the weight compressing the air decreases with elevation air expands, and in expanding absorbs from the surroundings heat which becomes latent because doing the work of expansion. On returning to a lower level this latent heat is given off again when the air reaches its original volume. Dry air falls in temperature about 1° F. for every 183 feet of elevation. When the air is moist this relation is disturbed by the latent heat set free from condensing watery vapor. Over the equator continuous snows are found on mountains at an altitude of 18,000 feet. The snow level north and south descends with increasing latitude, and varies with the season. Mountain tops are said to be cooler than the free air about them, though the rate of temperature

decline is less on mountain slopes than in the free air, and over elevated table lands the temperature decrease is much more gradual.

Watery vapor follows the law of expanding gases and decreases per volume of air with ascent; moreover, the amount held in solution is reduced by the lowered temperature (see table, p. 251).

Solid particles, which form an adventitious but constant constituent of the atmosphere at low levels, decrease with ascent above the surface. The air upon high mountain slopes has been found free from dust and bacteria. The result of these conditions has more physiological than physical value. Vegetation is sharply limited, owing to the falling temperature on the slopes of high mountains, as shown by the "timber line," which is higher on southern than on northern exposures.

Pure, dry air is nearly diathermanous. Solid particles, carbonic acid, and especially water in suspension are the atmospheric elements capable of absorbing heat. We therefore find that their reduction in elevated regions is manifested by increased intensity of insolation. A surface capable of absorbing heat becomes excessively warm under the sun's rays, but, the air being cold, a thermometer placed in the shade shows a low degree of temperature. The heat-absorbing constituents of the atmosphere also operate specifically upon the less refrangible rays of the spectrum. Therefore, solar heat and light are not only more intense in the clear air of high altitudes, but the proportion of "chemical" rays is greater than at sea level.

Soil.—The nature of the soil found in any locality is an important climatic factor. Soils differ greatly in their capacity for absorbing and radiating heat, and for holding water. Estimating the capacity for heat absorption and radiation of sandy limestone at 100, that of pure sand is 96, that of various clays varies from 67 to 77, while that of humus is only 49 (36). It has been found that a layer of sand half an inch or more thick on marshy ground so increases its absorptive power that the radiation at night suffices to prevent the freezing of crops that would otherwise suffer. The greatest range of temperature is found where the land has the greatest power of absorption and radiation, as over deserts. The character of the soil has especial importance in its relation to the absorption and retention of water. Sand absorbs water most readily, but allows it to percolate rapidly. Therefore, a sandy surface quickly dries after a heavy rain, unless underlaid by an impervious layer. Clay absorbs water with difficulty, and gives it up slowly. Humus has extraordinary capacity for absorbing water, which it takes up slowly, but retains strongly. Damp soils are those which retain or prevent the percolation of water. Cultivation of the ground greatly enhances its capacity to store water. The atmospheric humidity varies with the moisture in the soil, and the temperature relations of the air approach in equal degree those found over water surfaces. The reflecting powers of the ground

covering are of physiological moment, as witnessed in the glare from sandy deserts on the one hand, or mountain snow fields on the other.

ELECTRICITY.—Electricity is a climatic factor of unknown value. It is said that the atmosphere is usually positively electrified with regard to the earth, and that the open air is positive to that within dwellings. During rain storms the air charge is said to become negative. In the dry air of elevated regions the house dweller is often painfully reminded of his electric potential by the shock that follows his touch of a grounded conductor.

There may be truth in the popular conception that ozone has important climatological relations. It is a powerful oxidizing and purifying agent. It is formed from oxygen under the influence of electric discharges produced by many and various meteorologic and telluric conditions, or by the action of ultra-violet rays. In general, its presence indicates the absence of organic pollution, and is associated with a bracing physiological effect of the air.

COMPOSITION OF THE ATMOSPHERE.—The composition of the free air in different places is remarkably uniform. This is given for pure dry air by Moore (29) in the following:

TABLE SHOWING COMPOSITION OF THE ATMOSPHERE

	By Volume	By Weight
Nitrogen	78.04	75.46
Oxygen	20.99	23.19
Argon	0.94	1.30
Carbon dioxide	0.03	0.05
	100.00	100.00

Other gases, such as krypton, neon, etc., which occur in small amounts, are without known effect. A small trace of ammonia, important to plant life, is said to be normally present. A most important and variable constituent is watery vapor, which ranges in amount from 3 per cent. of volume in the dampest regions, to a vanishing proportion in the dryest. The percentage of the different components of the atmosphere, with the exception of the watery vapor, is practically unchanged by altitude.

BAROMETRIC PRESSURE.—This is the sum of the partial pressures of all the gases in the atmosphere. While the total pressure is due to and measures the total weight of the air-cone supporting the mercurial column, the partial pressures of the various components of the air do not exactly measure their relative weights. "Equality between partial pressures and weights would hold if the percentages of the gases present re-

mained constant throughout the atmospheres; but when the percentage of any substance decreases with elevation, the pressure it exerts is correspondingly greater than its own weight. Thus the pressure of water vapor at the surface of the earth is about six times its weight, or sixfold what it would be if the gases were not present" (29).

The atmospheric pressure at sea level in fair weather is usually represented by a mercurial column 760 millimeters, about 30 inches, high. The pressure decreases regularly with altitude, but its decline is affected by latitude, temperature, and humidity. The barometric fall for equal ascents becomes slightly less with increasing altitude. Roughly estimated, the barometer falls 1 mm. for every 12 meters ascent, or one inch for each 328 yards above sea level.

Dust and Impurities in the Atmosphere.—The hygienic relations of atmospheric purity will be referred to later. Except in the uninhabited regions of high altitudes, and to a degree over the oceans, dust particles, including microorganisms, are constantly suspended in the air. "The air of large cities invariably shows hundreds of thousands of dust-motes to the cubic centimeter, that of the village or town thousands, and that of the open country at least hundreds" (29). Light striking upon the suspended dust particles is scattered in all directions. They are the chief elements in the diffusion of daylight. In dust-free air only objects would be visible which were illuminated by the direct rays from the sun or those reflected from visible surfaces. Tyndall (43) found in his experiments that the dust most difficult to remove was combustible, and therefore composed of organic matter.

The color of the sky, the duration and colors of twilight, are largely determined by the optical effects of dust-motes in the upper air. But dust owes its particular climatological importance to the fact that its particles serve as the condensation centers which seem to be necessary to initiate the formation of droplets of moisture which give rise to fog, cloud, rain, and snow.

The Influence of Vegetation on Climate.—Forests have an important human interest in their efficiency as wind brakes. Radiation and evaporation are increased over verdure-covered areas and, therefore, the general influence of vegetation is to cool the soil. The average humidity of the air of forests is several degrees above that of that of the open. The general effect of such growths is to conserve uniformity of temperature and moisture and to oppose extremes. Only a few years ago it was generally assumed that vegetation, and especially forestation, had extreme importance both in increasing rainfall and in improving the capacity of the soil to absorb and retain water. Deforestation has been charged with causing aridity of once fertile regions on the one hand, and with allowing the rapid run off of excessive precipitation in disastrous floods on the other. An unprejudiced analysis of climatologic facts has led to the

conviction that vegetation in general is only an effect and not a cause of rainfall (17).

Professor Willis L. Moore, Chief of the U. S. Weather Bureau, has carefully investigated this subject (30).. He finds that: "In New England, where deforestation began early in our history and has been extensive, the mean of the fluctuations in the rain curve is a steady rise since 1836 up to a few years ago; and in the Ohio Valley, where the forest area has been greatly diminished, there is no decrease of rainfall shown by the average of the fluctuations of the curve." He concludes: "Precipitation controls forestation, but forestation has little or no effect upon precipitation. . . . The runoff of our rivers is not materially affected by any other factor than the precipitation. Floods are not of greater frequency and longer duration than formerly." It appears that the capacity of soil to absorb and retain water is enhanced rather more by artificial cultivation than by mere vegetation.

On the other hand, the existence and distribution of plant life are directly dependent upon temperature and humidity. Good crops are raised by "dry farming" in regions, as Colorado, where the rainfall is insufficient to support spontaneous growth. The main feature of the method consists in fine trituration of the surface soil. This conserves its moisture, probably in several ways, one of which may be, as Phillips suggests, the breaking up of the capillary pores through which drainage of surface water is wont to occur. The distribution of plant life in general, other things being favorable, is determined by temperature ranges. Plant growth does not take place until a temperature of about 43° F. is reached. The amount of growth depends upon the number of hours in a season in which the temperature is above this limit. Of two places having the same mean temperature, one may be barren and the other contain a rich flora through favor of a short, hot summer.

PHYSIOLOGICAL AND MEDICAL CLIMATOLOGY

The living organism responds to its physical environment. While each climatic factor has a preponderant effect upon one or another physiological function, the fact that these functions are interdependent and that climatic conditions vary more or less as a whole makes the study of physiological climatology one of exceeding complexity. The ideal scientific presentation of the subject would denote the relations between climate and the living organisms in the form of an equation. On one side would be grouped the physical variables entering into the concept climate; on the other side would stand the infinitely complex community of reacting cells of the body. The science of medical climatology must attempt to present the integral effects upon the second term of the equation of mutations in the variables of the first. This underlying mathematical concep-

tion of the subject is manifest in the actual examination by the laboratory worker of the physiologic effect of the change of individual climatic factors. Moreover, the mathematical point of view has definite practical value in that it reveals the futility of expecting a solution of the problem without a full knowledge of all the variables which enter into it.

The Physiological Reaction to External Temperature.—Temperature is biologically the most dominant factor of climate. Metabolism of living matter goes on within a narrow range of body temperature. Cold-blooded animals, whose chemical processes in large measure rise and fall with external temperature, have, like plants, a geographical distribution strictly related to the thermal environment. Warm-blooded animals react to variations of external temperature in such a way that, in general, metabolism with production of heat is increased and loss of heat decreased by external cold, while the reverse reactions occur when the external temperature rises. By these means a nearly constant body temperature is maintained under wide fluctuations of air temperature.

The heat of the body is due to katabolism, or the breaking down of complex into simpler chemical compounds, in which process potential energy becomes liberated and kinetic. The food is the fuel which supplies the body with all its energy, and there is believed to be an exact equality between the energy, estimated as heat, lost to the food in the body and that set free in the vital processes, supposing the weight of the body to remain the same. Therefore, the body in its metabolism is subject to the law of the conservation of energy.

Observations on men confined in a calorimeter show exactly how much energy, estimated as heat, is lost to the body under different conditions in a given time. It is obvious that, to maintain the body unchanged, it must receive in the food at least as much energy as it loses in its metabolism.

For the full value of food, etc., see Vol. I, Sec. I, Chapter XIII.

Parallel with the increased ingestion of heat-producing food, physiological combustions are increased in the cold, otherwise the level of body temperature could scarcely be maintained. The four-fifths or more of the energy of muscular contraction which appears as heat, not to speak of the warmth from circulation friction, are important sources of bodily heat. All these facts harmonize with the ethnic experience that, broadly speaking, the peoples of the higher temperate latitudes are characterized by physical energy and mental initiative, while those of torrid zones exhibit a comparative bodily lassitude and mental inertia.

In actual climates other factors than temperature, notably humidity of the air, enter into the physiological problem and demand a special discussion.

External temperature has a fundamental causal influence on body metabolism. It is a fair assumption that there is an optimum metabolism

at which machine efficiency of the organism is at its acme, and that this condition represents the most perfect attainable standard of good health for the individual. It seems probable, though it does not follow of necessity, that the ability of the tissues to adjust themselves to varying environment, and to produce the various biological antagonists against infectious diseases, should manifest an intimate dependence upon this physiological efficiency. In short, what we term "the resistance powers" of the body probably vary in some direct proportion with that harmony of metabolism whose optimum is manifested by perfect mechanical efficiency. Such a view finds luminous exposition in the clinical experience that an environment of open air provides the body with a more or less specific resistance against the advance of certain infections—notably tuberculosis. It is commonly admitted also that tuberculous patients thrive better when they react to the cold of winter than when subjected to the heat of summer. It is fundamentally important to realize that the community of living cells forming the body is a moving system, reacting instantly to every change of environment. The resultant of such a physiological adjustment is subtended by a state of consciousness, a sense of comfort or discomfort, of well-being or ill-being. This psychological condition is what determines man's estimate of climate, and I assume that it is the natural and, on the whole, most reliable test of the conservative or destructive tendencies of underlying physiological activities. Our appreciation of a change is always measured by the state to which we have already become adjusted. Thus, as Huggard points out (25), Ross and his party of Arctic explorers found the temperature of —29° to —25° F. agreeable after they had been exposed to one of —47° F.; and Parry's men complained of heat at 26° F. after they had become accustomed to —13° F.

Zuntz (48) and his party in the Alps found that, in the spring time, after a winter's inactivity, the guides suffered fatigue and metabolic disturbance in climbing a certain height, which disappeared after the physical training of a summer. *Training* is the process of physiological adjustment necessary in passing from one habit or environment to another. Every organism has its individual range of physiological response to the process of training. Somewhere on this scale, whether it be constructed on the basis of external temperature or any other climatic factor, is a point at which, for the moment, is found the optimum of physiological response—or that response which best conserves the well-being of the organism as a whole. The numerical situation of this optimum varies with the individual, and for the same person at different times. Beyond the extremes of the scale, life can no longer exist.

The essential thesis of this argument is that climate, in its broad sense, is an indispensable factor in physiological therapeutics.

The body temperature in man has been found by most observers to

vary only within one degree during residence in opposite extremes of latitude (35). The accuracy of most observations is impaired because the records have been obtained from the mouth or axilla. This uniformity of body temperature under different external conditions is maintained by coördination between the nervous mechanisms for the dissipation and production of heat. According to Vierordt (24), the relative loss of heat through various channels is represented in the following table:

1.	By urine and feces..........	1.8	per	cent.	or	47,500	calories
2.	By expired air: Warming of air	3.5	"	"	"	84,500	"
	Vaporization of water from lungs	7.2	"	"	"	182,120	"
3.	By evaporation from skin....	14.5	"	"	"	364,120	"
4.	By radiation and conduction from skin	73.0	"	"	"	1,791,820	"
						2,470,060	

The relative values of these factors change greatly with external temperature and humidity. Thus, in warm weather, the loss of heat resulting from the evaporation of perspiration rapidly augments. The nervous mechanisms involved comprise the respiratory center, the vasomotor center, the sweat centers, certain other secretory centers, and the various afferent and efferent nerves which connect them with the skin. The regulation of heat production involves chiefly the motor nerve centers with the motor nerves of skeletal muscles, and the character and quality of the food ingested. Calorimetric experiments on men and animals show that the respiratory exchange, measured by the amount of oxygen absorbed and carbon dioxid exhaled, increases with fall of external temperature. In the case of man, the increase of oxidation through cold is insignificant if, by voluntary control, muscular movement and shivering are avoided. Thus is manifest the purpose of the instinctive muscular activity induced by falling temperature. Rubner (24) found the amount of CO_2 eliminated by a fasting guinea-pig in air cooled to 0° C. to be more than double what it was when at a temperature of 34.9° C. (94.8° F.); and this with a difference of but 1.2° C. in body temperature.

The general conclusion from numerous researches on this subject is that the intake of oxygen and output of carbon dioxid increase with lowering, and decrease with rising, temperature of the environment. It is an interesting conclusion of Loewy that "the only involuntary regulator of temperature in a man exposed to moderate cold is the skin" (35). But the range of this coördination has definite limitations. Thus, both in man and animals, when the temperature of the calorimeter exceeds 30°

to 35° C. (86° to 95° F.), the combustions of the body increase beyond their magnitude at 20° C. (68° F.).

It seems very doubtful if such increased metabolism would be found in acclimated individuals living in the tropics. Pflüger made the interesting observation that, in a curarized rabbit, in which the muscles cannot be innervated, the gas exchange rises and falls with the external temperature as it does in cold-blooded animals. The same effect was obtained in paralysis following section of the spinal cord in the neck. It is a matter of medical interest to know that several observers agree that anesthetized mammals respond like cold-blooded animals to alterations in external temperature.

The investigation of the effects of climatic temperatures, especially in the tropics, on physiological functions offers considerable difficulties. The conditions in hot countries are prone to be complicated by parasitic infections. Thus, according to some observers, a decided degree of anemia characterizes the inhabitants of hot countries, the number of red corpuscles in the blood falling to half that normal in temperate zones. On the other hand, denizens of polar regions are said to show plethora and polycythemia (25).

These conditions might be explained by abundant alimentation on the one hand, and parasitic infection on the other. The influence of warm countries seems to lower arterial blood tension. The rate of heart beat at the same time does not seem to be materially changed. Evidence, of doubtful value, obtained at surgical operations and *post-mortem* examinations, indicates that residence in the tropics induces a hyperemia of the abdominal organs; on the other hand, the lungs contain less blood than usual.

The general physiological effect of residence in hot countries seems to be epitomized in the muscular and nervous lassitude reported by residents. The tendency is to a reduction in physiological tone; a lack at once in inhibitory force, and in active energy.

Physiological Influence of Atmospheric Humidity.—The watery vapor diffused through the air has extraordinary physiological importance, not through specific action of its own, but by modifying the effects of other climatic agencies, as heat, cold, wind, and light. The vapor of water in the air, like a body of water upon the earth, tends to the preservation of uniform temperature. Watery vapor absorbs and renders latent a great deal of heat. The warmer the air the greater its capacity for sustaining vapor, and thus accommodating a reserve of latent energy which must again become active when the vapor is condensed. Through atmospheric humidity the earth is thus screened from the extreme intensity of solar insolation by day, and the earth is protected from extreme chilling through radiation and evaporation at night. The air in contact with a cooling surface is suddenly warmed when dew is precipitated. As al-

ready mentioned, the drying power of the air is measured by the percentage of watery vapor which it lacks toward saturation; that is, it varies somewhat inversely with the relative humidity.

It has been seen that the regulation of body temperature in man involves the regulation of the loss of heat by the skin. In cold weather the skin is relatively dry and the radiation of heat is reduced by proper clothing, and the body warmth is conserved on the principle of the domestic "fireless cooker." As the external temperature rises, the skin circulation increases, and the sweat glands give forth their watery secretion. The evaporation of the sweat removes the excess of heat from the body. When the air is still, the relative humidity of the layer next to the skin is quickly raised so high as to impede further evaporation, the air seems "muggy," and the subjective sensation is one of profound discomfort. A gentle breeze brushes away the moist coating, and the refreshing cooling process continues. A stronger wind, especially when concentrated on a limited portion of the surface, is apt to occasion such rapid chilling as to cause widespread circulatory disturbances, which introduce a diversity of pathological conditions. Herein is a field for investigation which includes numberless phenomena, from the stiff neck that follows a draft, to the long list of respiratory infections that have some relation to surface chill. The discomfort occasioned by localized cooling of the body gives rise, in many people, to an instinctive aversion to drafts of air, which is worthy of special inquiry. Howell (24) quotes a case from Zuntz of a man who possessed no sweat glands: "In summer this individual was incapacitated for work, since even a small degree of muscular activity would cause an increase in his body temperature to 40° C. (104° F.), or 41° C. (105.8° F.)." This wonderful capacity of the body to regulate its temperature by evaporation was shown in the familiar experience of Blagden and Fordyce, published in the eighteenth century. These observers tested their own temperatures in rooms heated to various degrees. They found that the effect depended on the humidity of the air. "Thus, after remaining fifteen minutes in a damp room heated to 54.4° C. (129.9° F.), the temperature of the mouth and urine was 37.8° C. (100° F.), but in a similar exposure in a dry room heated to 115.5° C. (239.9° F.), to 126.7° C. (302° F.), and in which beefsteaks were being cooked by the heat of the air, did not raise the temperature of the body above the normal" (35).

It is clear that the chief regulator of the body temperature, as external heat increases, is evaporation of perspiration, and that the rate of evaporation is closely dependent upon the relative humidity of the air. The sensory nerves of the skin give fine warning of insufficiency in the physiological regulation through disagreeable sensations which we ascribe to "mugginess" or "stuffiness" of the air, and which are remedied, as will be seen later, by air renewal through "ventilation." When the external

temperature falls much below that of the body, atmospheric humidity still has predominant interest, but in another direction. When the air is cold and its humidity high, the skin loses heat to the moisture by *conduction,* which accounts for the peculiarly chilling effect of damp, cold air. Wind hastens this loss of heat, so that it is clear how the wind may make a hot day more tolerable and a cold one less so.

Ventilation.—Perhaps the greatest clinical discovery of all time is the empirical determination of the hygienic and therapeutic value of the open air. We are not yet certain of the physicophysiological reactions which constitute the virtue of fresh air.

Until recently it seemed clear that the subjective appreciation of air purity was a question of lung ventilation. It was taken for granted that the "bad air" of a closed and crowded room exerted its influence through a rise in CO_2 tension and fall in O_2 tension within the alveoli of the lungs. Moreover, it was held that the expired air contained organic excretions which imparted to it poisonous qualities. In short, the deleterious effects of respired air were attributed to its chemical qualities. But Haldane and Priestley (14) showed conclusively that, under a constant atmospheric pressure, the tension of CO_2 in the alveolar air remains practically constant. The slightest increase in such tension automatically stimulates the respiratory center to more vigorous action; "a rise of 0.2 per cent. of an atmosphere in the alveolar CO_2 pressure being, for instance, sufficient to double the amount of alveolar ventilation during rest." When a person under observation was made to rebreathe the air exhaled, he felt no abnormal subjective impressions until the CO_2 percentage in the air inhaled began to exceed 3 per cent. These authors found also that diminution of oxygen in the inspired air produced no reflex effect on respiratory rhythm until its pressure fell to about 13 per cent. of an atmosphere, which corresponds to an alveolar oxygen pressure of about 8 per cent. of an atmosphere, instead of a normal percentage of 11 to 17 (Loewy). It is therefore obvious that, as regards its content of O_2 and CO_2, the alveolar air is not only practically identical outdoors and in, but that under ordinary conditions its variations make no impression on consciousness. Many years ago Brown-Sequard and D'Arsonval announced that the deleterious qualities of expired air depended upon poisonous organic matter contained in it. They condensed the moisture in the breath of animals and injected the fluid obtained into other animals with fatal effects. Other observers, repeating these experiments, failed to obtain the same results. Finally, the whole question was submitted to an elaborate critical, experimental review in 1895 by Billings, Mitchell, and Bergey (6). These authors concluded that the ill effects of respired air depended wholly on its temperature and humidity, and not upon its increased content of carbon dioxid or any organic inclusion. Very recently, however, the subject has been taken up again by Rosenau

and Amoss (38), who have been able to demonstrate that the air exhaled by a human being actually contains organic matter, proteid in nature, emanating from the body. These authors, like most others, found that the condensed moisture of the breath produced no symptoms when injected into guinea-pigs. When, however, a little blood serum from the same person was injected after an appropriate interval of some days, the animal usually showed unmistakable evidence of anaphylactic shock. It had been sensitized by proteid contained in the fluid first injected. These results seem conclusive evidence that expired air contains organic matter. Whether this matter, when rebreathed, is physiologically indifferent, or whether it is resorbed and produces anaphylaxis, through which tissue resistance might be abnormally lowered by every subsequent exposure to breathed air, or whether, if resorbed, complete immunity to the substance is finally established, these are problems of great importance, and no final teaching on ventilation will be possible until they are solved.

From a noteworthy series of researches performed by Paul, Heymann, and Ercklantz under the direction of Flügge (11, 12, 20, 34), the conclusion seems justified that the subjective impressions that we have been accustomed to ascribe to disturbances of lung ventilation really depend upon modifications of skin ventilation. The observations were made upon men confined in a closed chamber of three meters capacity provided with an electric fan. When the air was kept in motion by the fan, the subject under experiment remained free from unpleasant sensations in air which, measured by ordinary standards, was excessively foul. When the fan was at rest and the air still, the person confined in the chamber soon began to suffer from the headache, dizziness, fatigue, nausea, etc., characteristic of extremely poor ventilation. In this condition the patient was allowed to breathe, through a tube fastened in the wall of the chamber, pure air from outside. No relief was experienced through this procedure; nevertheless, when the fan was started and the air put in active motion, the person under experiment again became comfortable.

Experiments by Leonard Hill (22) and his colleagues have confirmed, in the most positive way, Flügge's contention, that the subjective impressions aroused by lack of ventilation in closed spaces are nowise dependent upon the chemical constitution of the air breathed, but rather on its temperature and its humidity, which interfere with the heat regulation of the body by restricting transpiration from the skin. The beneficent influence of the air current is manifestly dependent chiefly upon the accelerated evaporation which it causes. The profound psychophysiological influence of temperature sensations derived from the skin is further evidenced by the curious fact observed by Boycott and Haldane (7), that when the air, whatever its real temperature, gave the impression of warmth of an unpleasant kind, the tension of CO_2 in the lung alveoli became lowered. They write: "We think, indeed, that it is one of the

physical expressions of the feeling of warmth and slackness, while the rise in the CO_2 tension (in the alveoli) is associated with the general exhilaration and stimulation produced by cold air."

Rosenau and Amoss (38) write: "Benedict has kept persons in his calorimeter breathing and rebreathing the same air with a CO_2 content as high as two per cent. for twenty-four hours without discomfort, the only precaution being to keep the temperature down and to remove the moisture."

Hough (23) describes an experiment in which a subject was confined for an hour or more in an air-tight box: "The percentage of CO_2 rose to 50 or more parts per 10,000. When the observer opened the door the odor of the air within was almost overpowering; and yet, provided the water vapor was absorbed and the temperature of the box kept down, the subject of the experiment had not only been unconscious of this odor, but had actually suffered no discomfort." In his excellent essay this author clearly indicates the physiological relations of atmospheric humidity with rising temperature. When the air temperature rises above 70° F., the body temperature would become elevated, but for the evaporation of perspiration. "When, however, owing to high humidity, evaporation is lessened, blood rushed in large quantities to the skin *at the expense of the flow to other organs;* the temperature of the skin is raised, and so heat transfer by radiation, conduction, and convection is facilitated. The normal temperature of the body is approximately maintained; but it is at the expense of the working efficiency of other organs, and especially that of the brain. . . . In these facts we probably find the true explanation of the dull, heavy feeling, the difficulty of attention, and the discomfort both of the muggy summer day and of the crowded, ill-ventilated room. . . . Humidity influences the output of heat from the body in two very different ways: It increases the conductivity of the atmosphere for heat—a cooling influence; and it interferes with the evaporation of perspiration—a heating influence. What the net result will be depends upon which of these influences of humidity is predominant." It is pointed out that at air temperatures between 68° and 70° F. neither high nor low humidities have marked physiological effects while the body is at rest. This, therefore, is the optimum range of temperature for maintaining the comfort of inhabited rooms.

Huggard (25) quotes from Humboldt a striking description of the physiological conditions produced by hot, damp climates: "We had not yet been two months in the hot zone, and already our organs were so sensitive to the slightest change of temperature that, through shivering with cold, we were unable to sleep; and to our astonishment we saw that our thermometer registered 21.8° C. (71.24° F.). . . . A change of not more than 7 or 8 degrees sufficed to bring about the opposite sensations of shivering and oppressive heat."

It is obvious from the foregoing discussion that the temperature, humidity, and motion of the air combine to determine physiological reactions, which are of the utmost significance to the welfare of the body. Though the discomfort aroused by the atmosphere of a poorly ventilated apartment may not, as demonstrated, be due to chemical deterioration of the air, nevertheless these sensations of ill-being lose none of their value for hygienic prophylaxis. The clinical experience which has demonstrated the debilitating effects of long-continued confinement in close air, as opposed to the invigoration attendant on life in the open, finds a ready explanation in the respective influence exercised by the two environments over the general resistance powers of the body. It appears that the skin is a peripheral sensory organ specifically concerned in maintaining the hygiene of metabolism.

The Physiological Influence of Diminished Barometric Pressure.—The mean pressure of the air at sea level may be assumed to balance a column of mercury 760 mm., about 30 inches, high. The total pressure is the sum of the partial pressures of all the components of the atmosphere. With elevation above sea level the fall in the barometer is measured by the mass of air left below. The rate of fall is approximately 1 mm. Hg for every 40 feet of ascent in free air, or one inch per 1,000 feet. With ascent the relative proportion of the constituent gases is maintained, except that the watery vapor is chiefly confined to the lower levels. Mere difference in atmospheric pressures appears, within wide limits, to be indifferent to living beings. The tension of the gases dissolved in the body fluids soon balances that of the surrounding air, so that the physiological phenomena of a rarefied atmosphere cannot be properly ascribed, as so often is done, to a suction-pump effect upon the pulmonary apparatus; although, it is true, a given amount of gas confined in the intestines expands in proportion to diminution of external pressure (21).

The importance of the time element in the adjustment of internal to external gas pressure is well illustrated in the phenomena of "caisson disease." In subaquatic constructions workmen in caissons are sometimes subjected to air pressures of three or four atmospheres. On returning to normal conditions, if the decompression is too rapid, peculiar symptoms, tingling, cramps, etc., are experienced, and paralysis or even death may ensue. *Post-mortem* examination shows that air emboli are set free in the central nervous system, leading to "necrosis in the region of the posterior and lateral columns of the cord, especially in the cervical region" (21). Such pathological results are avoided by slow decompression covering a period of 1-2 hours. The physiological effects of high altitudes are probably all to be explained by the lowered pressure of oxygen, and possibly of carbon dioxid also, in the alveoli of the lungs. In the dry atmosphere, at 760 mm. pressure, the partial pressure of oxygen is about 159 mm. That of carbon dioxid is negligible.

Zuntz and Loewy * analyzed the air expired by human beings and calculated that the composition of alveolar air varied between the following limits: "Oxygen between 11 and 17 per cent. of an atmosphere"; carbon dioxid between 3.7 and 5.5 per cent. of an atmosphere. Or, in terms of tension, the partial pressure of oxygen ranged between 83.6 mm. Hg and 129.2 mm., while that of carbon dioxid varied from 28.1 mm. Hg to 41.8 mm. Attention has already been called to the demonstration by Haldane and his associates that, under ordinary conditions, the partial pressure of CO_2 in the pulmonary alveoli of a given person is remarkably constant. A very slight increase in the CO_2 tension leads to hyperpnea and exaggerated elimination of CO_2 from the body; while, on the contrary, a lowering of CO_2 tension induces physiological apnea, or respiratory rest, and consequent accumulation of CO_2 in the body. That is, CO_2 is the normal stimulus of the respiratory center (19). On the other hand, fluctuation of oxygen tension in the alveolar air may occur within wide limits without producing obvious reaction. Nevertheless, when the partial pressure of oxygen in the atmosphere falls to a certain level, about 13 per cent. of an atmosphere (14), the tension of the gas in the lung alveoli is so lowered that the body cells suffer from the lack of oxygen.

Physiologists have generally maintained that the respiratory exchange between the alveolar air and the blood was regulated wholly by the physical law for diffusion of gases. According to this law, a gas must pass from a medium where its tension is higher to one where it is lower, until there is equilibrium of tension. But Haldane and Smith (15) maintain that the tension of oxygen in the blood leaving the lungs is much higher than that in the alveolar air, and, therefore, "Diffusion alone does not explain the passage of oxygen from the air of the pulmonary alveoli to the blood." In recent, unpublished, researches carried out on the top of Pike's Peak, Colorado, altitude 14,100 feet, Haldane,† Henderson, Douglas, and Schneider have apparently fully confirmed the view that active absorption of oxygen by the alveolar epithelium is an important, if not the only, force behind its appropriation by the blood, when the O_2 tension in the alveolar air falls below a certain critical tension (19). It has been shown by Zuntz and others that the suboxidation of the tissues resulting from a critical lowering of alveolar oxygen tension is accompanied by the accumulation of acid substances, especially of lactic acid, in the blood. These acid substances in the blood stimulate the respiratory center and lower its "threshold of irritability" for CO_2, so that the center is excited to work under the stimulus of a lower tension of CO_2 in the blood than would normally be effective.

It seems probable that this metabolic disturbance, which is particu-

* Quoted from Howell (24).

† Personal communication.

larly prone to affect newcomers in high altitudes, is directly responsible for many of the phenomena, especially of a psychic nature, of *mountain sickness.* Mountain sickness is a curious symptom-complex manifested in very various degrees by people who mount comparatively suddenly to high altitudes. In Europe the disorder is said to commonly manifest itself at elevations as low as 9,800 feet. In America the critical level seems to be considerably higher. The subjective symptoms are those of dyspnea, especially with exertion, and a feeling of oppression in the chest.

Disgust for food and nausea leading to vomiting give name to the disorder. The sufferer is absorbed in his own misery, and the mental disturbance may proceed to temporary alienation. The skin and lips are blue, the circulation and respiration distressed, and the slightest exertion exaggerates intolerably all symptoms. The inhalation of oxygen gas relieves at once, for the time, the morbid condition. After a quiet sojourn of two or three days at the altitude provoking the sickness, the body usually becomes accommodated to the new conditions, and a fair amount of exertion may be taken without undue distress. Cyanosis of the skin disappears, the lips again become red, and pulse and respiration return to about normal. A review of the literature on mountain sickness would reveal a curious multiplicity of explanations for the disorder. The dogmatic statement may be ventured that the final cause of the symptom-complex lies in an inadequate oxygen supply. Haldane and his colleagues on Pike's Peak found that, when samples of the venous blood were shaken up with air drawn from the alveoli of the lungs, the blood remained dark, although, at the same time, the arterial blood must have been bright red, as shown by the color of the lips and mucous membranes of the subjects. This experiment indicates both that the oxygen tension in the alveolar air was at least no greater than that in the blood from the right heart, and also that active absorption of oxygen by the alveolar epithelium must occur under such conditions.

Clinical experiences have led the writer to suspect that an important factor, if not the internal exciting cause, in mountain sickness lies in circulatory disorder resulting in accumulation of blood in the venous system through inefficient cardiac action, proceeding to dilatation of the right heart, and, in extreme cases, to insufficiency of the tricuspid valves. It is easy to believe that anoxemia would early depress the cardiac function. This would inevitably lead to plethora of the lungs and general venous system, and provoke the clinical symptoms characterizing the disorder. Unfortunately no opportunity has yet occurred to experimentally try out this theory, as by a study of the jugular and liver pulsations.

Physiological study of persons and animals removed from low to high altitudes shows a profound alteration in metabolism, especially of the

hemopoietic system. The absolute and relative amounts of hemoglobin and of the red blood-corpuscles are greatly increased at high altitudes. Zuntz and his colleagues (48), working on Monte Rosa, altitude 14,960 feet, showed that the activity of the red bone marrow, as shown by its hyperemia and increased number of nucleated red cells, was accelerated by low barometric pressure. The number of red blood-corpuscles has been found to rise from 5,000,000 at sea level to 8,000,000 at about 14,000 feet. The hemoglobin increases by 20 to 30 per cent. or more under the same conditions.

Reflecting on the reason for these changes in the blood, at first view there might seem a paradox of Nature in the provision of an excess of oxygen-carrying material in proportion to the diminution of oxygen to be carried. On the other hand, the conception is incontrovertible that the hemoglobin of the body is not only a carrier, but a storehouse, for oxygen; and the excess, or *luxus,* of this stored oxygen must be greater, the lower the oxygen pressure in the alveolar air, in order to meet the demands of muscular activity. The relation of this respiratory "factor of safety" (28) to the nutritional demands determining a physiological dietary, touched upon in a preceding section, is not without suggestiveness. Barcroft and King (4) have experimentally demonstrated the probability of hemoglobin serving, in certain lower animals, as a storehouse for oxygen, which is given up to the tissues as emergencies arise. The dissociation of oxygen from its carrier is greatly accelerated with rise of temperature (4), and it is highly probable that the elevation of temperature occurring in active muscles is a definite device of Nature to make loose the oxygen when needed.

As regards the colorless corpuscles of the blood, G. B. Webb (45, 46) and his associates at Colorado Springs, altitude 6,100 feet, find that there is a relative and absolute increase in the number of lymphocytes, including especially the large mononuclears, in the blood of persons removing from lower to higher altitudes. They find that the proportion of lymphocytes rises from an average of 37 per cent. at sea level to 44 per cent. at Colorado Springs, and to 54 per cent. at Pike's Peak.

O. M. Gilbert (13) of Boulder, Colorado, has repeated these observations at various altitudes varying from 9,000 feet above to 120 feet *below* sea level (in the Salton Sink of California). He found the highest ratio of lymphocytes (43.5 per cent.) in the blood of persons residing below sea level. At Boulder, elevation 5,380 feet, the proportion of lymphocytes was 42.6 per cent.; at Phœnix, Arizona, 1,100 feet, 41.5 per cent.; at Gold Hill and Ward, Colorado, 8,300 to 9,200 feet, 40.5 per cent.; at Aurora, Ill., 500 feet, 38.8 per cent. In short, the results indicate that the lymphocytosis is not a function of altitude *per se,* but of humidity of the atmosphere. The largest proportion of lymphocytes was found below sea level, where the air is phenomenally dry. This conclusion, if

confirmed, will add to the list of metabolic activities dependent on stimuli arising from the skin under the influence of heat and moisture.

The writer views "mountain sickness" as an expression of physiological incoördination accompanying an effort of the body to adjust itself to a new environment. It can hardly be doubted that the process of physiological adjustment to rising altitudes begins at levels far below those at which the pathological phenomena are excited. When a person ascends from a lower to a higher altitude and remains at rest, eating lightly and securing good elimination, the utmost physiological economy is secured, and metabolism usually adjusts itself without conscious disturbance to the new physical conditions. But when the newcomer to high altitudes is imprudent in diet, and especially when his mental exhilaration stimulates to over-exertion, the difficulties to physiological adjustment are, as pointed out in the preceding lines, enormously increased, and we can but expect an expression of incoördination. In healthy individuals the strain of accommodation is surmounted without serious ill-effect; but in persons suffering from organic insufficiencies, such as witnessed in active pulmonary tuberculosis, myocardial disease, renal disorders, etc., it is not uncommon, even at the elevation of Denver, one mile above sea level, for fatal results to follow casual imprudence in exercise indulged in before the process of acclimatization is completed.

The active readjustment of physiological powers accomplished during the period of acclimatization excellently illustrates the *rationale* and importance of *training* for one who would submit his organism to unusual strain of any sort. The admirable researches of Zuntz and his co-workers (48) definitely established the physiological value of training. Comparing the metabolism in trained and untrained subjects in climbing like heights, they found the energy evolved to be extraordinarily greater in the latter. A course of training largely eliminated this waste of energy. These accurate observations confirm the impressions gained from clinical experience, that unacclimated persons may usually sojourn with impunity in moderately high altitudes if careful not to over-exercise, but that the physiological effort in accomplishing a given amount of work increases somewhat inversely with barometric pressure. It is obvious that invalids visiting an elevated region cannot be too careful in avoiding physical exertion during the period of acclimatization, and that every unusual feat should be gradually reached through a course of training. Especially important among the facts determined by Zuntz and his co-laborers is the discovery that metabolism is modified so that there occurs an actual laying on of proteid tissue. This favorable change may begin at elevations as low as about 1,600 feet; but in ascents exceeding 6,000 feet the reverse process may become manifest. There tends, in untrained persons, to be an excessive consumption of proteid tissue. The favorable variation of metabolism initiated in moderately high altitudes may continue for a period after descent to lower levels. In the language of therapeutics, the characteristic salutary effect of elevated regions is tonic-reconstructive. Every climatic factor associated with low barometric pressure tends to act as a physiological stimulus to call forth latent powers and develop those already in action.

Insolation.—In high altitudes the intensity of insolation is great because the air holds but little moisture to absorb the rays; for the same reason, the heat radiated from the earth is not retained near the surface, but penetrates to upper levels. There is great difference, accordingly, between the temperatures of day and night, and between sun and

shade. In winter an invalid may sit comfortably in a solar temperature of 90° to 100° F., while a thermometer hung in the shade within arm's reach registers below the freezing point. As it is the shorter wave lengths of solar energy which are especially subject to atmospheric absorption, the light of elevated regions is peculiarly rich in these "chemical" rays. The intense illumination is probably largely responsible for the psychic restlessness and irritability often witnessed in unacclimated persons at high altitudes.

The physiological and psychic influence of light make it a climatic factor of great importance. Major C. E. Woodruff (47) charges the intense solar illumination with the evils, especially of the nervous system, which make difficult the residence of white people in the tropics.

According to him, light is the important agent in the production of neurasthenia and multifarious allied nervous disorders, and persons of blond complexion are especially subject to its evil influences. It seems highly probable that the debilitation induced in the tropics is due rather to the combined influences of heat and humidity, than to excessive illumination. Light is indispensable to normal life, and, if its excess leads to physiologic disturbance, it becomes all the more imperative for the climatic therapeutist to specifically consider this agent in his recommendations. It has already been stated that *temperature* takes the first rank in determining the physiological relations of climate. But it has long been clear that the *feeling* of heat, or "sensible temperature," may vary widely from the air temperature as measured by the ordinary thermometer. Prof. M. W. Harrington (18), former Chief of the U. S. Weather Bureau, was apparently the first to definitely point out that the sensations of temperature run much more nearly parallel to the readings of the wet-bulb than of the dry-bulb thermometer.

Accordingly, in dry air, in which the heat of the body is carried away by evaporation or perspiration, the weather may be comfortable, when at the same air temperature in a humid locality the heat would be oppressive. Wind movement greatly enhances evaporation and the cooling effect of dry air. Isotherms plotted from readings of wet and dry-bulb thermometers, respectively, differ widely in their course, and we find therein a physical explanation of the surprising coolness felt on entering the shade on a summer's day in arid regions. In the winter, on the other hand, by reason of the low humidity, little heat is lost to the body by conduction. Therefore, resorts in elevated regions tend to seem much cooler in summer and warmer in winter than places on the same parallel near sea level (42).

Prof. Cleveland Abbe (1) points out that different individuals respond variously to the same physical environment, as does one and the same person at different times, as before and after eating. Observing

his own sensations, with the wind blowing five miles an hour, he noted the following results:

Temperature	Relative Humidity	Subjective State
80° F.	20	Feels fine
40°	60	Feels fine
20°	80	Weather very raw
60°	80	Comfortable
80°	100	Suffocating

In an essay like this it is impossible to give a detailed discussion of the modification of physiological functions induced at high altitudes. The monumental works of Paul Bert (5), of Mosso (31), and of Zuntz (48) and his collaborators, together with the researches which have been cited here, represent the essentials of our present knowledge of the subject.

Dust and Atmospheric Impurities.—Impurities in the atmosphere in the form of dust and noxious gases, not to speak of bacterial and other contaminations, have undoubtedly great, though little investigated, effect on human health. The lungs are the organs specifically affected. The solid particles inhaled, to a greater or less extent, penetrate the bronchial mucous membrane and are distributed thence by the lymphatics, leading to a condition known as *pneumonokoniosis*. Fibroid changes are induced by irritation from the foreign particles, and considerable areas of the lung tissue may be replaced by solid nodules, or masses of deeply stained fibrous tissue. Chronic bronchitis and emphysema are the characteristic clinical sequences. The familiar "miners' consumption" is anatomically a pulmonary fibrosis. In the lungs of a stone-cutter, forced to abandon his occupation on account of increasing dyspnea, the X-ray plate showed me dense shadows radiating from masses at the roots of the lungs, and involving the greater portion of the organs. There was no evidence of tuberculosis in this case. Lungs so affected seem to lose much of their normal immunity against bacterial infection. In the mining regions of Colorado it is not uncommon to find superb athletes suddenly succumbing to an intractable form of pulmonary tuberculosis. It is not improbable that the high mortality from pneumonia witnessed in similar districts is likewise associated with dust inhalation. The intimate effect of inorganic inclusions on the vital resistance of the lungs is emphasized by J. M. Anders (2), who quotes Scurfield's observations on occupation mortality in Sheffield; the death rate of "grinders from phthisis is more than six times, and the death rate from other respiratory diseases nearly three times, that of the average male; while the death rate of cutlers from phthisis is nearly three times, and from other respiratory diseases nearly four times, that of the average male." The quality of the foreign matter inhaled seems not to be indifferent; thus, according to Osler (32), coal

miners are not especially subject to phthisis. In his experiments on dust Tyndall (43) found the air exhaled toward the end of expiration to be free from solid particles, a fact significant of the amount of dust that must be retained. In manufacturing centers the smoke from burning coal, composed chiefly of carbonaceous particles with a considerable content of CO_2 and SO_2, probably has important relations to the public health. The sulphurous acid is especially irritating to the respiratory mucous membrane. Under the action of oxygen and moisture it becomes converted into sulphuric acid. F. W. Schaefer (39) calculates that there are daily discharged from chimneys into the air of London about 300 tons of soot, 90,000 tons of carbon dioxid, and 2,700 tons of sulphur dioxid.*

These bodies are all much heavier than air and tend to settle. The solid particles, at least, form foci for the condensation of moisture, so that fogs, impregnated with the gases of combustion, are readily generated. Statistics show that morbidity and mortality from respiratory diseases are greatly increased during heavy fogs in manufacturing districts. It has been calculated that steel dust from the brake-shoes of moving trains formerly permeated the air of the New York subway to the extent of one ton in a mile of the tunnel. The hygienic importance of this subject must be greatly enhanced when, to the inorganic dust, are added putrescible substances and pathogenic microorganisms. Moreover, if the conception of atmospheric pollution is broadened to include not only inert suspensions, but the living insects which transport infectious matter, control of the purity of the air must banish much of the disease which now afflicts mankind. Wind and rain are the natural purifiers of the air, as regards accidental contaminations.

The Psychology of Climate.—The demonstration within the past half century that the law of the conservation of energy applies to the metabolisms of the living body led to a mechanical view of vital processes which only incompletely represents the forces that control the human being. But the mental state is still refractory to mathematical exposition, and practical clinicians are turning back to that viewpoint of Life from which the mind is regarded as an ever-acting and often predominant energy in physiological processes.

Military medical officers in foreign fields assert the disastrous influence of nostalgia in patients afflicted with ailments which at home would be considered comparatively trifling.

Madden (27) writes: "The Stagyrite, who knew all things and treated of them and some others, makes excellent observations on the indispensable necessity of serenity of mind, hopefulness, and even cheerfulness, for health of soul or body." When the change of climatic stimuli relieves ennui, awakens an interest in Nature, or excites zest for mental

* The figures reported probably should be modified as the result of the application of smoke consuming devices.

effort, it tends to produce that cheerful serenity of which Aristotle recognized the value. This phase of medical climatology is as pervading as it is elusive of analysis; the principles of climatic treatment are founded on psychology as well as physiology.

The Classification of Climates

This difficult subject has been treated by Dr. W. F. R. Phillips (36) in a comprehensive table, of which the following is a copy:

The Classification of Climates

Classification basis	Subdivisions under classification	General characteristics of each subdivision
Solar or Astronomical	Tropical	Usually mild, equable, moist, warm, average temperature 80° F. Rainfall frequent and heavy over water and over windward land exposures. Nights usually clear, afternoons cloudy. No general storms. Seasons rainy and dry; but this division is only a relative one.
	Temperate	Unsettled weather, great and variable changes in temperature, rainfall and moisture from season to season and day to day. Region of cyclonic storms, cold and hot waves, floods and droughts.
	Arctic	Cold; temperature on average considerably below freezing. Scanty rainfall. Very short but hot summer. Winter long and severe. Storms infrequent.
Geographical	Continental	High temperature in day time, low at night. Difference between day and night temperatures increases toward center of continent. Great variations in temperature, sometimes hot, sometimes cold. Moisture variable from almost saturation to aridity. Rainfall subject to great variations and extremes. General tendency to extremes in all climatic elements.
	Oceanic	Temperature equable, range between day and night hardly exceeds 2° to 4° F. in mid-ocean. Moisture high but constant. Rainfall frequent.
	Insular and littoral	Intermediate between above, partaking more or less of the characteristics of one or the other.

THE CLASSIFICATION OF CLIMATES—*Continued*

Classification basis	Subdivisions under classification	General characteristics of each subdivision
Topographical (land)	Plain	Extremes of temperature great, rainfall uncertain, humidity low.
	Hill	Extremes of temperature less than plain, rainfall greater, humidity higher.
	Mountain	Generally same as hill, except effects of altitude become more evident; rainfall increases up to about 5000 ft. then decreases.
	Valley	Extremes of temperature greater than hill. Humidity greater; rainfall greater than plain.
	Desert	Rainless; great extremes of temperature between night and day and season and season.
	Artificial	Such as climates of large cities. Temperature of cities always higher than surrounding country. Haze, cloud and fog more frequent.
Aerophysical	Temperature	High, Intermediate, Low: According to the degree of heat adopted as the standard of comparison.
	Humidity	Damp or moist, Intermediate, Dry or arid: According to the standard of humidity adopted.
Physiological	Invigorating, Relaxing, Rigorous, etc.	According to the general effects of the particular climate.
	Mild, Pleasant, Humid, Disagreeable, etc.	According to the general sensations produced, etc.

The foregoing table illustrates the fact that climatic characters may be grouped around various points of view. The therapeutist conceives the climatic conditions likely to be remedial for his patient, and tries to select them in some definite place, with due regard to local medical and sociological advantages. There is no lack of excellent climatic guide-books of descriptive medical topography.

THE APPLICATION OF CLIMATE TO THE TREATMENT OF DISEASE

It would seem, at first sight, easy to determine from empirical observation the climatic conditions remedial for various pathological states. But experience shows that benefits which had apparently been originally

derived from the climate of some definite locality finally ceased to reward the seekers of health; so that factors other than those of climate were brought into consideration. Resorts for the tuberculous, for example, that once seemed salutary, have time and again developed into hotbeds of the disease. No fair estimate of the physiological influence of the tropics, for example, can be made until infections incidental to the hot zone are under sanitary control. In short, the causes of disease must be understood before a scientific application of climatic therapeutics can be hoped for.

Again, unnecessary obscurity has been thrown round the subject of physiological climatology by the frequent failure to recognize that, in every place, many of the physical factors of climate are subject to immediate artificial change, to a degree which it would require long journeys to realize by geographical means. Temperature, humidity, air movement, insolation, are largely subject to artificial regulation.

The one disease the treatment of which inevitably involves a consideration of climatology is

Tuberculosis.—When the pathogenic organism of tuberculosis was discovered, the last doubt was removed as to the reason why resorts which originally seemed favorable to recovery from the disease so often proved later to be danger spots for its acquisition.

Pace the claims for the remedial powers of tuberculin, the years have yielded but one indispensable agent in the prevention and cure of tuberculosis—the open air. It is curious how little the crudity of this clinical finding has been refined. We have been at a loss for definite explanation of the hygienic virtues of open as compared with closed air. Referring to a preceding discussion on the physiology of ventilation, the contention of Flügge seems sustained, that the morbid sensations through which we recognize the impurity of respired air are not due directly to acquired chemical properties of the air, but to the irritation of certain sensory nerves of the skin brought about by a rise of temperature combined with a high degree of relative humidity. The nerves specifically concerned in these sensations would seem to be those delegated to temperature sensations; moreover, in the clothed subject, the skin of exposed parts, the head, neck, hands, wrists, possibly the lining of the nasal canal, would seem to be of relatively paramount importance. In explaining the maintenance of a constant body temperature under wide thermal variations of the air, we find no difficulty in ascribing profound alterations in metabolism to stimuli arising in the temperature nerves of the skin. From the same point of view the suggestion is obvious that the sensations of comfort or discomfort aroused in "good" or "bad" air are but incomplete conscious expressions of tissue reactions which determine the molecular efficiency of the machine, and incidentally regulate the production of substances protective against disease. While heat and humidity are of pre-

dominant importance in the excitement of cutaneous sensations leading to feelings of well- or ill-being, it would be a too narrow view which would restrict to the action of these physical agents the multifarious sensory impulses, largely operating through the consciousness of pleasure and pain, through which the metabolisms of the body are, I venture to believe, largely ordered.

Thus "Nature," through visual and auditory impressions, especially, tends to generate what might be called an esthetic state, which is a potent addition to that mental atmosphere which favors recovery from tuberculosis.

It is worth while, in passing, to point out that the response of the body to the manipulations of hydrotherapy is, in large measure, but a demonstration of the physiologic influence of temperature and moisture on cutaneous sensations.

These reflections point to a physical basis for the known physiological effects of life in the open, and make it conceivable that all the advantages of such an environment might be secured indoors under artificial regulation of temperature, humidity, air movement, illumination, and other factors, physiologic and psychic, which enter the play of the outside climate.

In short, the facts point to the conclusion that the "resistance powers" of the body, aside from those specific immunities developed in response to substances in the circulation, are developed as reactions to afferent nerve impulses, or sensory impressions, which spring for the most part from the cutaneous surface.*

The victim of pulmonary tuberculosis, thrilled with sickening chills along his spine, is prone to huddle over a stove in a closed chamber, or to seek relief in a land of perpetual summer. But practical clinicians have long since found that recovery from the infection is apt to be furthered rather in a somewhat variable and rigorous than in an equable climate; and it is the general testimony from health resorts that patients commonly do better in winter than in summer. It is profoundly significant that the same patient who, left to his own devices, had dreaded a fall of air temperature below 72° F., under proper therapeutic control learns to rejoice in the crisp, freezing air of a northern winter. His point of view has been so altered by training, that his feelings of pleasure and pain resume their normal function as sentinels to conserve his well-being. He breaks the vicious circle in which a morbid sensation led to a hurtful act.

For the specific indications for the application of the open-air treatment in pulmonary tuberculosis see Vol. II, Sec. I, Chapter XXV.

* There is an analogy between the action of these trophic afferent impulses and that of the biochemic antigens which stimulate the tissues to produce immune bodies. Cf. the suggestive paper by Crile (10).

When the conception obtained currency that the open air was the most salutary environment for the consumptive, a tendency was manifested by certain phthisiographers to estimate, as of equal therapeutic value, all open air, and to decry the hitherto assumed virtues of climatic change. While admitting that the climate of the back yard was more remedial for the tuberculous than the climate of the adjoining kitchen, they would not grant that a still greater deviation in meteorologic conditions to be found in distant resorts could have healing virtues in excess of those to be found on a city lot. This question can only be decided empirically; but the Reason cannot but be impressed with the physiological facts of climate, such, e. g., as the specific stimulation of the blood-forming organs, of tissue proteid assimilation, etc., which occur in moderately high altitudes. The unbiased mind must grant, at least, that every climatic complex operates for or against the recovery of a consumptive in proportion as it excites conservative or destructive physiological reactions. The impression has gained ground that a cure of tuberculosis at high altitudes leaves the patient especially liable to relapse, or to again contract the disease, on returning to lower levels. It is probable that the only truth behind this belief is the fact that many cases of arrested pulmonary disease can pursue a useful life under certain favorable conditions and no others. The tendency of persons returning home, after achieving arrest of their disease, is to abandon the hygienic methods to which they owed improvement. It is also true that the temperament and constitution of one who has harbored tuberculosis ofttimes demand the stimulating conditions of high altitude to maintain a feeling of well-being, which of itself must be a powerful aid to the resistance powers. The body is probably vastly more sensitive to the influence of environment and is subject to a wider variety of physical stimuli than we have any idea of. An experimental analogy for this position is offered by the exceedingly suggestive results obtained by Reid Hunt (26), in his investigation of the "Effects of a restricted diet and of various diets upon the resistance of animals to certain poisons." He found that the resistance of some animals to certain poisons may be increased forty-fold by changes in diet; the converse effect may follow an appropriate dietary. The resistance of animals to the poison investigated was apparently directly related to certain internal secretions, particularly that of the thyroid gland, whose production is modified by diet. "Season has an important effect upon the resistance of animals to certain poisons; in some cases these effects seem to depend upon seasonable variations in the activity of the thyroid."

In an essay like this only general relations of climate to special diseases can be touched upon. The works of Huggard (25), Solly (42), and others must be consulted for details.

Anemia.—Efficient operation of the blood-forming organs is a funda-

mental requirement for health. Aside from the specific effect of infections, the state of the blood has a very direct relation to climatic environment. Residence in the tropics seems to induce anemia, whereas removal to an invigorating climate restores the blood. The work of Zuntz, Haldane, and others, on high altitude physiology, seems to demonstrate that the diminution of oxygen tension in the air specifically stimulates the bone marrow, and probably other sites of blood formation, to excessive activity.

Therefore, even at moderate elevations of 3,000 to 5,000 feet, the red blood count and the hemoglobin percentage exceed those of people at sea level. At high altitudes health demands a proportionate increase of hemoglobin and red corpuscles. In somewhat crude clinical observations at Denver, one mile above sea level, I have been accustomed to find disorders attributable to anemia in patients whose hemoglobin percentage ranged as high as 70 per cent. to 85 per cent.

Gout.—Gout and lithemic states are due to conditions of metabolism and circulation which are modified by climatic treatment. According to Huggard, "a dry, bracing climate is always most suitable." Nevertheless, the writer is convinced that a characteristic effect of residence in high altitudes, at least in the unacclimated, is a relative venous plethora. High venous blood pressure, according to good authority, leads to gout. Newcomers in moderately high altitudes, particularly if indiscreet in exercise, are apt to suffer from "bilious attacks" as a phase in acclimatization.

Rheumatoid Diseases.—Painful affections of the connective tissues grouped under the term "rheumatoid diseases" are common in high altitudes; their incidence probably bears an inverse proportion to the metabolic reactive power of the individual. On the contrary, *acute articular rheumatism* is probably much less frequent than at sea level.

Respiratory Affections.—*Catarrhal conditions and bronchitis,* as a rule, are most favorably influenced in a climate of moderate humidity. Newcomers in Rocky Mountain resorts habitually complain of irritative symptoms, which are due to drying of the mucous membranes.

Tuberculous laryngitis and other organic respiratory affections, though primarily contraindicating very dry air, not uncommonly in elevated regions find amelioration in the establishment of a general improvement in well-being. Theory and experience as a whole agree in the teaching that the mortality from *lobar pneumonia* increases in very high altitudes. Nevertheless, practitioners in moderately elevated regions will probably agree with J. N. Hall (16), who, from a wide experience, concludes: "I believe from this study that the mortality of acute pneumonia is not materially affected by altitude until one passes beyond an elevation of 6,000 or 7,000 feet."

Certainly the pneumonia morbidity and mortality in Denver are not in excess of those for the same disease at sea level.

One of the most curious of clinical experiences with *"bronchial asthma"* is the frequent complete relief afforded at elevations of a mile or so above sea level. On the contrary, the subjects of *emphysema* are not apt to do well.

Heart Diseases.—Heart diseases are benefited or made worse in high altitudes, in proportion to the power of the heart to respond to excessive demands upon it, and thus increase its range of accommodation.

The prescription of "mountain climbing" in the treatment of chronic heart disease has a sound physiological basis. Nevertheless, when a physician at an elevated resort finds it difficult to restore a broken compensation, he desires above all things to see his patient transported to a lower level.

While the body is at rest, the mechanical conditions of the circulation are practically identical through a wide range of elevation above the sea; but the demands of muscular exertion call for an increase of cardiac activity which is excessive in proportion to the altitude. Acclimatization, or training, greatly expands the limits through which the heart can adjust itself without overstrain.

R. H. Babcock (3) is probably correct in his assumption that the condition of mitral stenosis is one which, for mechanical reasons, especially contraindicates high altitudes. Nevertheless, in Denver, for example, many persons with stenosis of the mitral valve live in comfort. Nervous affections of the heart appear to be bettered or otherwise, in high altitudes, according to the general reactive powers of the patients.

There seems no reason for believing that, in patients who lead a quiet life, *arteriosclerosis* contraindicates residence in high altitudes. However, it appears that aneurysm and mortality therefrom are considerably greater at high than at low elevations (41).

Disorders of Digestion.—In the writer's estimation, climate is indirectly of importance in its impress on the digestive functions through its effect on the metabolic and nervous systems.

When the general condition of a patient improves, digestion is likely to take on normal activity, and *vice versâ.*

Especially in high altitudes, a "nervous dyspepsia" is apt to reflect imperfect adjustment to the environment; and a "bilious attack," which the writer has attributed to relative venous engorgement, frequently attends the process of acclimatization.

Skin Diseases.—Great importance has been attributed in the foregoing pages to the physiological functions of the skin. There is no organ of the body which comes so directly under the influence of climate as the skin, yet there appears to be but a meager collection of data regarding the subject, either in health or disease. Cases of *eczema,* at least in its

acute form, are said to do badly on the seashore, and in cold, damp weather. *Acne* is also made worse on the coast, and is apt to improve in dry inland stations. Cases with *psoriasis* do better in a warm climate.

It has been said that at high altitudes those cases do worse in which the skin disease depends on nervous derangement.

Disorders of the Kidneys.—It is generally admitted that the chief object to be secured in the treatment of kidney disease is rest for the organ. The potent factors within our control include diet, muscular exercise, and the activities of the skin and lungs. Experience indicates that patients with disordered kidneys fare worst in cold, damp places of variable temperature. They thrive best in warm, equable, and somewhat dry climates. There is substantial basis for the opinion that persons with inflamed or degenerated kidneys are apt to fare badly at high altitudes. In my experience, disease contracted at an elevation is better borne than when imported. It is difficult to acclimatize a diseased kidney.

The medical observer is impressed with the paramount importance of the circulation in renal insufficiency. Clinical experience has impressed me with the belief that passive congestion of the kidneys is the preponderant deleterious factor due to the conditions of high altitude. The subject, however, is a very complex one. There is reason to believe that certain forms and stages of kidney disease, as of heart disease, are distinctly ameliorated by a judicious mode of life at a moderately high altitude.

The Nervous System.—Special emphasis has been laid in the preceding pages on the purely psychic value of climatic change. The mental state is molded to a great degree by the reactions occurring in the various organs, among which the nervous system is of predominant importance. "Climates may affect the nervous system either directly or indirectly through their influence on metabolism in its widest sense. Using the rather indefinite terms in vogue, climates may be *relaxing, sedative,* or *stimulating* in their influence. When nutrition is improved and a state of well-being secured, the qualifying term *tonic* may be added. Thus, warm, moist coasts or islands are sedative to relaxing. On ocean voyages or cooler coasts the prevailing influence is tonic-sedative. Inland places of low altitudes are usually simply tonic in effect. Elevated inland regions are stimulating-tonic or simply stimulating" (40).

It has been made obvious that the physiological influence of high altitudes tends to increase the chemical activity of certain vital tissues. At moderate elevations, 4,000 to 6,000 feet, laying on of proteid tissue, building up of the organs, and improvement in their efficiency tend to occur. With further increase of elevation katabolic processes gain ascendancy, and it is as if the machine suffered from internal friction. It cannot be too strongly emphasized that physiological adjustment to lowered barometric pressure requires time and rest. Imprudence in exercise on

the part of newcomers is prone to turn a sojourn which might have been salutary into a period of nervous overstrain. Constitution and tempera-ment determine, to an extraordinary degree, the fitness of people for residence in elevated regions. Persons of phlegmatic disposition, or those who are nervous from malnutrition or overwork, are apt to do well at high altitudes. The hysterical and those with inherent nervous temperaments often find their disorders accentuated. Nevertheless, the medical ob-server is often astonished at the development of nervous stability in pa-tients whom, from a theoretical viewpoint, he would have advised against seeking a high altitude. The general belief that an occasional drop to sea level is necessary to the best interests of residents at high altitudes is probably well founded. Differences in temperament and constitution, which become especially conspicuous under the strain of low atmospheric pressure, no doubt determine, in a less sensible degree, the adaptability of people to other climatic conditions.

Thus, though we may not accept fully Major Woodruff's dictum that in the tropics, or brilliant sunlight, fair-skinned persons always deterio-rate in health, as compared with brunettes, it is nevertheless true that individual as well as racial characters determine to a large degree the adaptability of climates to the preservation of health and the cure of disease.

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CHAPTER VI

MASSAGE AND GYMNASTICS

Charles G. Taylor

MASSAGE

The term massage (of Greek derivation, meaning "to knead") was first used by the French to designate a systematic method of manipulating the tissues of the body for therapeutic purposes, such as modifying nutrition, breaking up adhesions, etc. This form of mechanotherapy has been used to combat morbid conditions of the body by the different races of the world for more than three thousand years. The Chinese were probably among the first to employ it, and it is extensively practiced by them to-day. In Japan the art is practiced largely by blind men, who, in spite of their infirmity, are very skilful operators. They are frequently summoned as they pass through the streets at night, making their presence known by a weird whistle. The ancient Greeks and Romans employed massage in connection with their famous baths. Hippocrates advocated its use, and in his works can be found references to its value as a therapeutic agent. Many other noted ancient physicians used it in one form or another, with marked success. The Hindoos and Persians were among the earliest races to recognize its value, and they are very apt in practicing it. Massage has only been used on the European continent for probably three hundred years, and then first in France. About one hundred years later it was recognized and adopted by the Germans, and then in England. The high degree of perfection to which the art has been developed we owe largely to the excellent work done by Ling of Sweden, Mezger of Amsterdam, and his pupils, von Mosengeil, Berghman, and Helledey.

It is only within the past twenty-five to thirty years that massage has been employed to any great extent in this country. For a long time the medical profession generally looked upon it as being of doubtful utility, and by many it was thought to be practiced only by charlatans and quacks. Unfortunately, this attitude did much to delay its development here. Dr. S. Weir Mitchell was among the first men in the United States to advocate its employment. Not until the introduction of his

famous rest cure, and the demonstration of the value of massage as an essential feature of it, was the subject given any serious consideration by the great majority of the medical men in the country. Dr. J. H. Kellogg has also done a great deal to encourage the intelligent employment of the art on this side, being the author of one of the best texts in English on the subject.

At the present time massage is a well recognized therapeutic measure, and has proven valuable not only in combating certain nutritional disorders, but also in some surgical cases. This applies to the treatment of fractures and to certain post-operative cases. When employed in connection with systematic exercises it is of value in the treatment of certain deformities, such as flat-foot, round shoulders, scoliosis, ankylosed joints, and contractures.

In order to become a successful masseur, or masseuse, it is absolutely necessary to have a practical knowledge of anatomy and physiology. Without these the procedure becomes one of simply rubbing the body at random, and the most satisfactory results cannot be expected. The operator should possess certain qualities of touch and gentleness which will enable him to manipulate the soft parts and joints without bruising the tissues or causing the patient the slightest discomfort. It is essential that he have a strong, healthy body to withstand the exhausting character of his work.

Technique of Massage

Since it is the chief purpose of this article to offer to the physician the indications for the employment of massage, only such details of the technique will be covered as will enable him to become familiar with the nature of the treatment his patient is to receive, and in a measure to judge the efficiency of his operator. For a more elaborate treatment of the subject the reader is referred to one of the larger texts.

The time devoted to massage of the entire body should depend upon the strength of the patient and the reaction produced. In delicate women it is usually best to begin with one-half hour and gradually increase a little each day. Ordinarily, however, one hour should be allotted for a thorough general treatment, the time devoted to the different parts being as follows: upper extremities, 15 minutes; lower extremities, 20 minutes; trunk, 20 minutes; head and neck, 5 minutes. The time given to local treatments will, of course, depend upon the nature and location of the condition to be treated and the object in view. For general massage an hour should be selected midway between the meal hours, or as nearly as is practical, and, following the treatment, the patient should remain in a darkened room for from forty-five minutes to an hour, to encourage rest and relaxation.

During the treatment the room should be well ventilated with a temperature of 65° to 70° F. The patient should lie between the folds of a light blanket, having first removed all articles of clothing. The utmost care should be taken to see that only such parts of the body are exposed as are under treatment at the moment. In order to avoid any irritation of hairy surfaces, the part should be lightly lubricated with cocoa butter, or vaselin, or other such substances. The operator starts with the feet and toes, and gradually works up the leg and thigh to the trunk, completing one limb before the other is commenced. Next the hands, forearms, and arms are treated, then the muscles of the back, the abdomen, the chest, neck, and head, in the order named. Ordinarily the face is not treated in general massage. The various procedures of manipulating the tissues as outlined below are used, first one and then another.

Inasmuch as joint movements constitute a part of the procedure in a general treatment, they will be considered here, although they are not, strictly speaking, a part of massage proper.

The manipulations employed consist of:

1. Stroking and friction.
2. Kneading.
3. Vibration.
4. Percussion.
5. Joint movements.

Stroking and Friction.—In the performance of these movements Fig. 1) the operator uses the tips of the fingers, the thumb, or the entire

Fig. 1.—Stroking.

palmar surface of the fingers and hand. The chief difference between stroking and friction lies in the degree of pressure applied. In stroking only very light pressure is used, sometimes even less than the weight of the hand, while in friction varying degrees are applied, depending upon the part and condition to be treated. Generally speaking, the direction

of the movements in stroking, in relation to the blood current, should be centrifugal, while in friction they should be the reverse, or centripetal.

FIG. 2.—FRICTION TO THE BACK.

There are several methods of employing friction, the one selected depending upon the part to be treated and the object in view (Figs. 2 and 3).

FIG. 3.—DEEP FRICTION TO ABDOMEN.

Kneading.—As one might infer from the term, kneading (Figs. 4 and 5) is the most important manipulation employed in massage. It consists of rhythmical compressions and relaxations of the soft parts, at the same time rubbing them together much as a baker kneads dough. It may

be either superficial or deep in character, some parts of the body requiring only the use of the finger tips, so-called "digital kneading," or, if a

Fig. 4.—Kneading.

fleshy part is under treatment, the entire hand is brought into play, "palmar kneading." The skin and underlying structures are firmly but

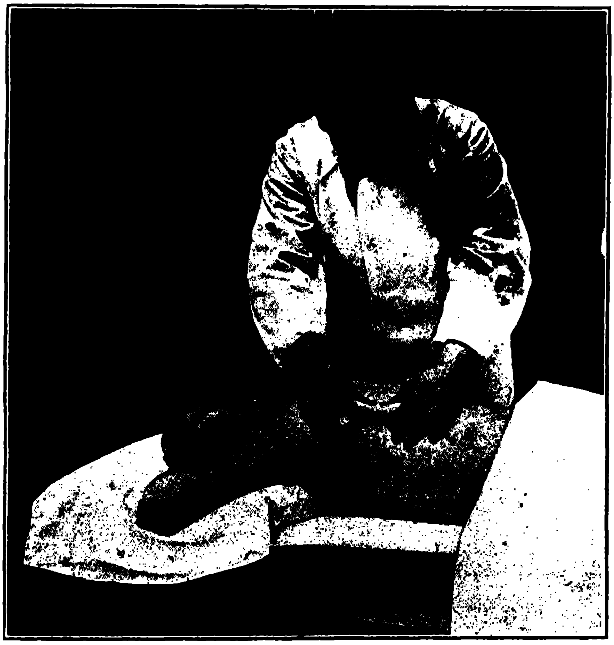

Fig. 5.—Kneading Back Muscles.

gently grasped in such a manner as to affect, primarily, the deeper structures and not the skin, as in stroking.

Vibration.—This consists of fine vibratory movements transmitted to the body of the patient by a rapid, shaking movement from the arm of

the operator. Vibration may be superficial or deep, and may be communicated to the subject by means of the fingers, the knuckles, or the palmar surface of the hands. Generally speaking, a very rapid vibration is most efficacious, and it usually requires a good deal of skill on the part of the operator.

Percussion.—Percussion means simply the imparting of carefully graduated blows to the body of the patient. This may be done in many different ways: by using the finger tips; the inner border of the hands with the fingers either apart or held together (Fig. 6); with the fist half

Fig. 6.—Percussion.

closed; by using the palmar surface of the hand; either flat or held in a concave or cup-shaped manner, so-called clapping or slapping. The degree of force used will depend upon the particular method employed and the part under treatment. The greatest care should be used to avoid bruising the tissues. The operator should permit of absolutely free movement of the wrist joint, in order to deliver a flexible, springy blow.

Joint Movements.—Skilfully directed movements of the joints of the body, whether performed by the patient (active) or by the operator (passive), afford a valuable method of exercising, not only the tissues immediately concerned in the structure of the joint, but also the muscles and tendons attached to and in close proximity to it. The movements employed may be any one, or all, of those which the structure of the joint will permit. These may include extension, flexion, adduction, abduction,

circumduction, and stretching. *Active* movements may be resisted by the operator, or *passive* movements may be resisted by the patient, in either

Fig. 7.—Passive Movements of Ankle Joint.

case exercising to a marked degree the muscles involved. An elaboration of the former constitutes the foundation of the Schott exercises for certain cardiac conditions. Simple *passive* movements, performed wholly by the

Fig. 8.—Passive Movements of Shoulder Joint.

operator and without any effort on the part of the patient, concern chiefly the structures of the joint and to a lesser degree the surrounding tendons and musculature (Figs. 7 and 8).

[All movements should be synchronous with inspiration and expiration.—Editor.]

Physiological Effects of Massage

Massage exercises a *local,* or mechanical, and a *general,* or dynamic, influence upon the human body. As the hand of the operator manipulates the tissues, the blood and lymph currents are accelerated even in the finest capillaries and smallest lymph spaces, and thus local stasis is relieved, and the chemical changes incident to anabolism and catabolism are encouraged. It therefore follows that the condition of the tissues locally is improved; the glands of the skin become more active, while the underlying muscular tissue improves in tone and develops more rapidly as a result of the increased amount of nutrition conveyed to these parts by the blood and lymph. There is likewise a nutritional influence exerted upon the fine terminal nerve filaments, which are rendered more capable of receiving and transmitting impulses. By means of the afferent nerve fibers, connected with the cerebrospinal and sympathetic systems, beneficial effects are produced upon related centers in a reflex manner, so that the entire bodily economy is improved. Massage favorably influences the circulatory and the respiratory systems; thus the ingestion of oxygen and the output of carbon dioxid gas are increased.

Effect Upon the Circulatory Apparatus and the Blood.—The rapidity and force of the heart beat are increased by general massage, and there is a slight temporary elevation of the blood pressure. When abdominal massage alone is given the heart beat becomes slower and more full. This is due to the fact that the intraabdominal pressure is increased as a result of stimulation of the vasoconstrictors of the abdominal vessels, and to stimulation of the abdominal muscles, two factors which serve to put a large part of the blood, always present in these parts, into the general circulation. The blood pressure is, therefore, elevated to a more marked degree, and is more permanent than when the entire body is treated, and the vessels of the other parts of the body are subjected to the same stimulating influences as those of the abdominal cavity. When general massage is given the superficial vessels of the extremities dilate and the blood rushes to the skin, producing an active hyperemia. The larger vessels in the deeper tissues share equally with those of the abdominal cavity in the stimulating effect derived, but the smaller vessels of the periphery take up the large amount of blood that would otherwise produce a more marked acceleration of the pulse and elevation of arterial pressure.

In addition to the increased activity of the circulatory apparatus, due

to the mechanical effect of manipulating the tissues, there is also a greater demand for the removal of waste products resulting from the increased oxidation as in exercise, and the blood is hurried on to the kidneys, the lungs, and the skin, to eliminate its toxins and carry nutrition to the cells.

As the passage of the blood through the vessels is augmented, the heart is reflexly stimulated. The myocardium receives its ration of nutriment and is rendered more capable of performing its function. Its contractions become strengthened and are rhythmical and full.

When it is desired to relieve a congested condition of any of the internal organs, or of the brain, a great deal can frequently be accomplished by treating the extremities. For instance, if one wishes to relieve the portal system of an abnormal amount of blood, massage of the lower, or of all four, extremities will favorably influence the circulation. With this object in view in a given case, it is best to use *stroking,* or very light *friction,* instead of the heavier procedures, as the former will dilate the superficial vessels without stimulating the deeper ones, and thus the blood is admitted to the outer recesses of the body and away from the site of the congestion.

Another factor that influences the circulatory apparatus is the lengthened excursions of the diaphragm produced by the stimulating effect of massage. Not only is the blood circulation augmented in this manner, but it has been definitely shown that the flow of lymph in the thoracic duct is increased. The effect of massage upon the lymph circulation is most marked, as the spaces which convey the lymph are particularly numerous in the subcutaneous tissues and between the muscles and the various organs of the body; this renders them very accessible for mechanical manipulation. The importance of stimulating the lymph flow is readily apparent when we remember that it serves to carry away a great deal of the débris and the toxins of constantly dying cells. It has been definitely demonstrated by von Mosengeil, Höffinger, and others that the absorption of liquids in the peritoneum and in joints, etc., is profoundly influenced by massage.

The effect of massage upon the composition of the blood is a very definite one. The number of red blood corpuscles in the circulation will be found to undergo a substantial increase within half an hour after a general treatment, and to persist for an hour or more. The oxygen-carrying capacity of the blood is thereby increased, as is the elimination of carbon dioxid gas. Upon first thought, one would naturally conclude that this increase in the number of cells in the periphery is due to the stimulating effect of massage upon the circulation, and that the additional cells come from the inner recesses of the body, particularly the spleen, liver, and long bones, where we know they are constantly stored in large quantities. This conclusion is, of course, a logical and correct one, but

there is also a definite influence produced upon the blood-making processes, as is clearly demonstrated by the permanent results obtained in certain anemic states when massage is given regularly. The percentage of hemoglobin in the red cells is also increased. This is notably the case in the treatment of chlorosis, where the deficiency in the coloring matter is the predominating feature of the pathological picture. Systematic massage, together with proper hydrotherapeutic methods, has proven of the greatest value in the treatment of this disease, and some authorities employ it to the exclusion of all iron preparations. In any depraved condition of the blood, general body massage given regularly every day will exert a markedly beneficial effect upon both the hemoglobin and the cell content.

The leukocytes of the blood are also increased by massage, and to a more marked degree proportionately, and with more permanency, than the red cells. The importance of this fact is at once obvious. Since we have to depend to a great extent upon the phagocytic properties of the white cells to keep the body free from the attacks of the constantly invading organisms, and to remove the débris of exudates, etc., any agent that will favorably influence their production must be of real value.

Effect Upon the Respiratory Apparatus.—Massage affects the respiratory apparatus by increasing the depth of the respirations, and to a very slight degree by increasing the frequency of the respiratory movements. These changes may be said to be due to two factors: one, the stimulation of the diaphragm—with the resulting lengthened excursions—and of the muscles concerned in the respiratory movements of the chest, both directly and reflexly; and, two, the increased demand made upon the lungs for the interchange of gases in the blood stream, resulting from the greater activity of the circulatory apparatus and the increased number of erythrocytes in circulation. Any atelectatic areas in the lungs are encouraged to normal expansion, and when massage is employed in connection with deep breathing and other exercises it proves a most valuable adjunct in overcoming deformities of the chest. The pulmonary vessels receive their ratio of nutriment from the blood, and the lung tissue is strengthened. The millions of germs that are constantly being inhaled are combated by the increased number of phagocytes present, and thus the resistive force of the body is raised.

Effect Upon the Nervous System.—There is probably no branch of medicine which offers so large a field to massage, and in which more satisfactory results have been obtained, than in the treatment of nervous disorders. Its usefulness may be considered under two heads: one, as a general body tonic and stimulant to muscular tissue; and, two, as a sedative. Since the skin and subcutaneous tissues are abundantly supplied with the fine terminal nerve fibers, it naturally follows that they are particularly susceptible to the influences of massage. Receiving the

stimulating effects of manipulation, and the increased nutrition from the blood stream, they are not only benefited locally, but stimulating impulses are transmitted along the afferent fibers to the central neural apparatus, from which other parts of the body derive a share of the effects by way of the efferent paths. As a result of the influence produced upon the sympathetic system, the vasomotor apparatus is affected; the superficial blood vessels dilate, and the hyperemia produced thereby increases the heat radiation from the body. In this manner the reat-regulating center is stimulated, and the body temperature is elevated. This effect upon the temperature of the body naturally promotes oxidation, so that every function is improved.

Sedative effects are best produced by terminating the treatment with gentle stroking. This enhances the feeling of euphoria that should always follow a general massage treatment, and the patient, other conditions permitting, will desire to sleep. In neuralgic conditions relief is frequently obtained by strong, rapid percussion. This procedure produces an anesthetic state of the nerve to which it is applied.

Effect Upon the Abdominal Viscera.—The digestive and eliminative apparatus are the principal organs of the abdominal cavity to be influenced by massage. The stomach and intestines are stimulated to increased activity, and their functions improved in three different ways. First, the muscular tissue of the walls is stimulated, and the peristaltic movements increased, so that their contents are moved along and stasis is overcome or prevented. Second, the vasomotor control of the vessels is improved, the intraabdominal pressure is raised, and the large amount of blood in these parts is forced into the general circulation, returning from the lungs with renewed vitality, and thus improving the nutrition of the parts permanently. Third, the glandular activity of the stomach and small intestine is increased, so that the food particles are more readily and thoroughly digested, and in the large intestine a greater amount of fluid is mixed with the contents, so that the expulsion of waste products finally is augmented. The more abundant supply of blood promotes the absorption and assimilation of food.

The liver, spleen, pancreas, and kidneys are all favorably influenced by abdominal massage, chiefly through the increase in the quantity and quality of the blood supply. The output of bile is increased both by the mechanical effects upon the gall-bladder and its ducts, and by the increased activity of the hepatic glands. The amount of glycogen released into the circulation is raised as a result of the increased oxidation going on in the body, and the liver makes greater demands upon the blood to supply fuel for its sugar metabolism. In congested conditions of this organ considerable relief is obtained by the stimulating effects produced upon the circulation. The spleen and pancreas are benefited in a similar manner, the cytogenic properties of the former being definitely influenced.

Effect Upon the Muscular and Skeletal Systems.—What has been said above in regard to the tonifying effects of massage upon involuntary muscle and other tissues of the body as a result of the greater nutriment afforded by the circulation, applies equally well to the voluntary muscular apparatus and to the bones and ligaments. When systematically applied to an atrophied and poorly developed muscle there follows not only marked improvement in its tone and contractile power, but a very definite increase in its size. This is due in part to the stimulating effects of the mechanical irritation upon the muscle tissue and its nerve terminals, but chiefly to the increased nutriment carried to the parts and the removal of fatigue toxins and waste products. The latter phenomena explain the readiness with which soreness and stiffness, resulting from excessive exercise, are relieved by massage. Massage exercises a muscle and keeps it in proper condition without the expenditure of nervous energy, hence its value in the treatment of conditions in which it is desired to rest the nervous system, at the same time not permitting deterioration of the muscles.

Since the medullary substance of the long bones is recognized as playing an important part in the production of red blood cells, it is apparent that an increase in the activity of the circulation in these parts would augment this function, as well as improve the nutrition of the bone substance itself.

GYMNASTICS

By gymnastics is meant systematic tissue exercise as a result of muscular effort. It is obvious, then, that gymnastic exercise is a definite form of massage, compressing and stretching muscle groups, nerves, blood vessels, organs, etc., in a definite and systematic manner.

Medical gymnastics were advocated and taught first by Peter Ling in his school in Stockholm in 1815, and to his successor Branting is due the credit for having worked out a most satisfactory understanding of the physiology of the art. August and Theodore Schott, of Bad Nauheim, have elaborated eminently satisfactory methods of applying massage and gymnastics, particularly in the treatment of certain cardiovascular conditions. The "Schott movements" consist of carefully graduated resistant exercises given by a skilled operator, who offers resistance to the movements of the patient, to a degree indicated by the condition of the heart and vessels and the amount of work desired to be placed upon the former. These exercises will be taken up in detail later. The high degree of efficiency of gymnastics as a therapeutic agency, particularly when combined with massage, should commend them to more extended usage. It is largely due to the determined efforts of the Swedes that we have a system of gymnastics which is being applied with universal success to

the preservation and restoration of health. Credit should be given, however, to the Germans and Americans for the proficiency to which the uses of medical gymnastics have been brought. The influence of gymnastics in the preservation of a properly functionating mind and body is plainly evidenced by the alertness of the rosy-cheeked and well-nourished school child. The varied endeavors of the playful youngster are forms of gymnastics which are essential to the growth and development of the body. By their rompings there is a general bodily massage which is a material aid to metabolism. There are deep inhalations of pure air, furnishing the necessary oxygen for the increased exchange of cell food and waste products. The latter are hurried along the venous capillary channels and into the larger veins, thence to the lungs for expulsion. The physiological activity incident to this accelerated interchange of gases obviates physical and mental dulness, and the various organs of the body are enabled to discharge their duties under more favorable circumstances. These natural gymnastic movements of the child are exercises of endurance rather than exercises of force, the principles of which should be incorporated in the application of gymnastics to pathological conditions.

Gymnastic exercises as applied in the schools of the present day are productive of the greatest amount of good. Perhaps it is not too strong to state that hundreds of lives are saved yearly by school gymnastics, and many more are saved from invalidism, most notably by lessening the frequency of the various tuberculous infections, such as pulmonary tuberculosis, Pott's disease, tuberculous arthritis, and osteomyelitis, etc. By raising the resistive power of the body, it is likewise fortified against the acute infectious diseases.

It should be constantly borne in mind that all exercises of endurance should be modified to the needs of each individual. The body weight is the best guide for this purpose. Exercises should be lessened in their vigorousness when there is a loss of weight, unless the object of such exercises is weight reduction, and increased when the body weight increases, provided the various physiological processes are properly functionating.

As gymnastics are applicable for the insuring of the proper functional activity of the organs and processes of the body in health, so they are, when skilfully modified, applicable for the improvement of function in pathological conditions. They are exercises of endurance, beginning in a very mild way and gradually adding more effort, that have the greatest general tonic effect; while exercises of skill have to do chiefly with the training and development of the nervous system. Efforts of strength rapidly develop muscular tissue. Exercises of force, as performed in a single act, have very slight influence upon the pulse, blood pressure, or respiration. If the act is repeated often, or if it is an act of continuous

muscular effort, as in lifting, the influence will be very great upon the cardiovascular and pulmonic systems.

Exercises which are applicable in the restoration of health are modifications of those which are employed for the preservation thereof. The degree of modification necessary will depend upon the strength of the individual and the condition to be overcome. In some pathological conditions there may be no, or only very slight, change advisable from the exercises which are best suited in conditions of health.

Gymnastic exercises should be divided into two main groups: those which are applicable in health, and those which are applicable in disease. Gymnastics in health are best divided into: school exercises, gymnasium exercises, and field exercises. In diseased conditions the exercises employed should be such as will exert their beneficial effects upon the pathological condition to be combated, whether it be of the cardiovascular system, the muscular system, or the correction of a scoliosis; hence it is impractical to offer any definite classification, and, therefore, each type of exercise will be treated individually.

Gymnastics in Health

School Exercises.—School exercises should consist of breathing exercises, calisthenics, marching, dancing steps, and playground exercises. Participants should be grouped according to the physical strength, and not according to age or class work grading. Some children are better developed physically at the age of twelve years than others are at fifteen, and a child of fourteen who is undeveloped could not perform tasks equal in physical effort to those performed by the normal child of fourteen.

Breathing exercises and calisthenics are easily and beneficially executed together. The pupils should be arranged in rows with ample room between each to permit of the free movement of arms and legs. The room should be supplied with as much fresh air as the windows and doors will afford. The time for inhalation and exhalation on beginning should be about fifteen seconds, gradually increasing the time a few seconds each day until, after considerable practice, one minute can be consumed in an act of inhalation, retention, and exhalation. This applies to pupils of normal development, who are fifteen years of age or older. For those under this age about half the time should be allotted to the exercise. All inhalations and exhalations should be executed evenly and slowly, and, while the lungs should be expanded to their fullest capacity, the amount of air taken in should not be sufficient to cause discomfort. It is well to have the class make a certain number of simple body movements during each respiratory act. These may consist of bending the body forward and backward and from side to side, or flexion and extension of the arms and legs, and of rotatory movements of the shoulder and hip joints.

For more detailed description of movements that may thus be employed see under "Diseases of the Respiratory System." A great variety of exercises may be found by consulting those books devoted to this subject, a list of which is given at the conclusion of this article.

Gymnasium and Field Exercises.—Gymnasium exercises consist of dumbbell, Indian club, and wand drills; pulley weight, horse, and bar exercises; rope and ladder work, rowing machine, and bag punching exercises; games, such as basketball, etc. These methods are designed to exercise, in a systematic manner, definite muscle groups, and are prescribed to develop certain parts of the body according to the needs of the individual case, or, when several or all of the different methods are employed, they serve to strengthen and develop the entire body. Field exercises consist of outdoor games; baseball, football, tennis, etc.; track work, such as speed and endurance races, hurdle races; feats of sudden effort, as the pole vault, high jump, hammer throwing, shot put, etc. Needless to say, all exercises should be taken in the open air when possible. In schools a good plan is to put the pupils through the daily calisthenic exercises in the school yard just before they are released for the first recess, and just before going home.

Gymnastics in Disease

The application of gymnastics to pathological conditions is effected by muscular effort on the part of the patient, with or without resistive manipulations by an operator, and by mechanical appliances. The subject of mechanotherapy will not be taken up in this consideration of gymnastics, as it is a more highly specialized form of exercise and is treated elsewhere in this work. The methods of applying exercises to various pathological conditions will now be considered.

THE APPLICATION OF MASSAGE AND GYMNASTICS TO PATHOLOGICAL CONDITIONS

Flat Foot (pes planus), Round Shoulders, Scoliosis.—The reader is referred to works on orthopedic practice for the mechanical treatment of these conditions.

Diseases of the Circulation

As would be expected, massage, which produces its effects mainly by means of the circulation, has a large and important province in the treatment of circulatory diseases. For indications see Vol. III, Sec. III, Chapter II.

Schott Movements

The Schott exercises are slow, even movements, resisted evenly and firmly by the operator; these are followed by a short period of rest after each exercise. By following this rule carefully any undue strain upon the heart is avoided. The condition of the pulse should be frequently noted, at first before and after each movement. Great care must be exercised in order that the patient does not become fatigued. There should be a feeling of freshness after each treatment; dulness over the heart and liver should gradually become less, and the pulse slower and of better volume. A slight degree of palpitation or of dyspnea should be an indication for the discontinuance of the exercises, and should serve to indicate the amount of exertion to be employed at a subsequent treatment. The following list of Schott movements are those given by Thorne ("Schott Method of Treatment"), quoted by McKenzie:

1. Spread the arms until they are in line at the level of the shoulders (Fig. 9). Bring them together (Fig. 10).
2. Flex the forearms (Fig. 11); extend the forearms (Fig. 12).
3. Raise the arms sideways, palms upward (Fig. 13), until the thumbs touch above the head. Sideways lower (Fig. 14).
4. Press together the knuckles of both hands with the fingers flexed at the second joint; raise the arms above the head (Fig. 15). Lower the arms to the starting point in front of the abdomen (Fig. 16).
5. Arms forward, raise vertically above the head (Fig. 17). Forward lower (Fig. 18).
6. Forward flexion of the trunk (Fig. 19). Extension (Fig. 20).
7. Trunk rotation to right and left alternately. Keep up even resistance, passing partially around him (Fig. 21).
8. Flex the trunk to the right and left alternately; straighten (Fig. 22).
9. This movement is identical with exercise No. 2, except that the fists are clenched (Figs. 11 and 12).
10. This movement is the same as No. 9, except that the arm is at the side (Figs. 11 and 12).
11. Rotate the arms forward, upward, backward, and downward.
12. Push both arms backward; draw them forward (Fig. 23).
13. Flex the thigh with knee bent (Fig. 24); relax, extend the thigh (Fig. 25).
14. Extend the leg and bring the extended leg forward (Fig. 26). Draw the leg backward (Fig. 27).
15. Flex the leg on thigh (Fig. 28); extend the leg (Fig. 29).
16. Abduct and adduct the leg (Fig. 30).
17. Arms extended horizontally; rotate forward and backward with resistance.

Fig. 9.—Exercise 1.

Fig. 10.—Exercise 1.

Fig. 11.—Exercise 2.

Fig. 12.—Exercise 2.

Fig. 13.—Exercise 3.

Fig. 14.—Exercise 3.

18. Extend the hand; flex the hand (Fig. 31).
19. Extend the foot; flex the foot (Fig. 32).

Satterthwaite has somewhat modified these exercises, and has arranged a scheme of detailed application for the first two weeks, the second two weeks, the third, etc.

The Oertel exercises are pedestrian exercises, and consist of walking on graded roads of increased steepness. A restriction of fluids is advocated. They were formulated by Oertel, of Munich, in the treatment of his own case, which was one of dyspnea, cyanosis, and edema of the legs, following the gradual development of obesity. The treatment is essentially an athletic training, and is especially indicated as a preventive measure. It is beneficial in cases of obesity, and in circulatory conditions where compensation has been already established. In the application of this treatment the patient must always be made to sit down and rest short of fatigue.

Diseases of the Respiratory System

Massage and gymnastics have found a place in the treatment of pulmonary conditions through their circulatory and nutritional effects. For indications see Vol. III, Sec. II, Chapter IV.

Breathing exercises, however, play the greatest part in the therapeutics of massage of the respiratory apparatus, and most of all are they applicable as a prophylactic measure. These are appropriately combined with gymnastics to heighten the effect. Such are the calisthenic exercises which have come to occupy a prominent part—and deservedly so—in our public school training. They are respiratory gymnastics, and as such they take their place among general measures for physical development, and safeguards against disease. Besides this, breathing exercises play the most important part in vocal training, and, while this may be one of the refinements of education, it nevertheless needs earnest consideration, especially in the light of the many major and minor speech defects which offer comparatively little resistance to early treatment. Thus, respiratory gymnastics may be divided into the same two groups as body gymnastics: the one group aiming to develop the organ physically by endurance, and the other functionally by skill or control. It is to the former that we now turn in its application to pulmonary disease.

The patient, in the sitting, but preferably in the standing, position, assumes an erect posture; the chin well up to permit free flow of air through the upper respiratory passages; the shoulders held well back to permit free and easy expansion of the chest. All clothing which tends in the slightest to constrict the thorax and upper abdomen should be removed. The arms are bent at an acute angle, with the hands (ulnar side downward) lightly but firmly resting on the lower thoracic wall. The

FIG. 15.—EXERCISE 4.

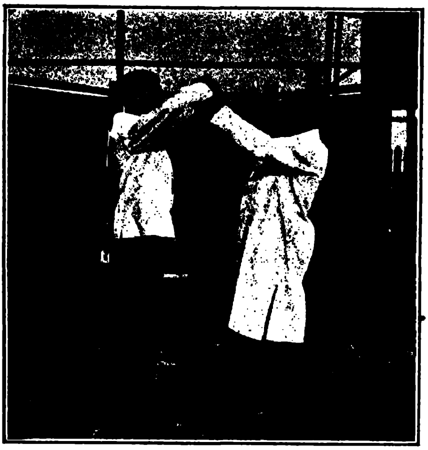

FIG. 16.—EXERCISE 4.

FIG. 17.—EXERCISE 5.

FIG. 18.—EXERCISE 5.

FIG. 19.—EXERCISE 6.

FIG. 20.—EXERCISE 6.

patient is then directed to concentrate his attention upon the expansion of his chest, and particularly upon the chest movements under his hands. Before the inspiration is taken the expiration is carried to the extreme, the hands aiding this process by pressing and constricting the underlying chest wall. Immediately upon the completion of expiration, inspiration begins. This takes place through the nose, and must be smoothly and gradually executed, the hands relaxing their pressure as the walls expand beneath them. The beginner may have difficulty in prolonging the time of the first inspiration to five seconds, but he soon acquires this control, and the duration should be gradually lengthened to fifteen or twenty seconds. The pause following this inspiratory act need be only a short one at first, and there is no advantage in increasing this beyond ten seconds at any time. Expiration then proceeds in like manner, slowly, smoothly, with attention constantly directed to the chest movements under the hands, and the gradual increase of pressure exerted by the latter as the expiratory act is completed; the duration should be increased from ten to thirty seconds. The lower abdomen is held moderately contracted; the shoulders should not be raised, nor the inspirations and expirations so extreme that the patient distorts his features. Above all, the respiratory movements should be rhythmically carried out, smoothly, not jerkily, and until a certain proficiency in execution is acquired no advance is to be considered.

This method of breathing is appropriate, as it affords a gradual expansion or stretching of the delicate lung tissue, there being no advantage here, and at least a theoretical disadvantage, in the rapid and more vigorous intake of air advocated in vocal exercises.

Breathing through the nose is also recommended, as this is the physiological method during not too violent exercise. And there need be no stress put upon the so-called diaphragmatic breathing, since all full expansion of the thorax is necessarily diaphragmatic, as Gutzmann has so clearly shown in his "Stimme und Stimmbildung" (Voice and Voice Culture).

When the above simple exercise has been properly performed, gymnastic movements may be combined, for their own sake and for the sake of diversion and concentration afforded by a greater variety of movements, which would otherwise become monotonous. These may be briefly described as follows:

Respiratory Exercises

1. Hands placed upon the hips; thumbs pointing backward; elbows moved forward, constricting the chest during expiration, and backward, giving free play for expansion during inspiration.
2. Arms extended forward, parallel and horizontal, with palms fac-

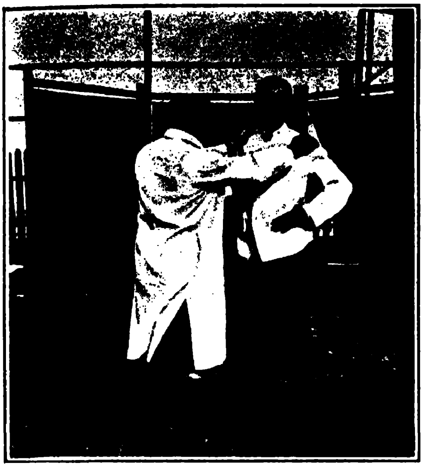

Fig. 21.—Exercise 7.

Fig. 22.—Exercise 8.

Fig. 23.—Exercise 12.

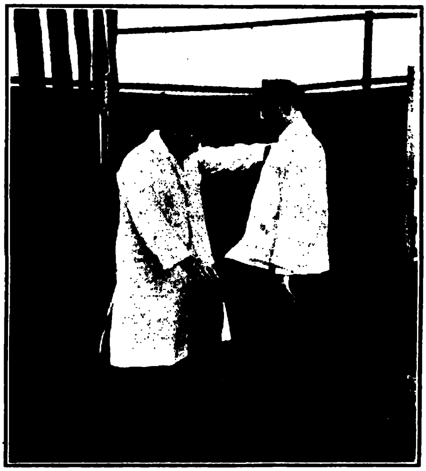

Fig. 24.—Exercise 13.

Fig. 25.—Exercise 13.

Fig. 26.—Exercise 14.

ing each other—expiration; moved backward to the extreme in the horizontal plane—inspiration.

3. Arms directed downward at the sides, palms inward—expiration; raise laterally to the perpendicular, turning the palms upward midway, until they face each other in the perpendicular and parallel position above the head—inspiration.

4. Perform circles with the arms extended laterally, the expiration taking place during the execution of the lower half of the circle (forward movement), and the inspiration during the upper half of the circle (backward movement).

5. With the hands on the hips, the body is bent forward from the waist line during expiration, backward during inspiration.

6. These movements may be assisted by forcibly but gently drawing the arms backward at the extreme of inspiration, the operator taking his position behind the patient and guiding his arms during the excursions.

Numerous other combinations of simple invention may be added, but the point which should be most strongly impressed and insisted upon in the performing of any of these exercises is exactitude—coördinating the calisthenic exercise with the two phases of breathing—not to have a breath half finished when the arms have reached the final position, etc.

Diseases of the Nervous System

As a palliative and curative measure for the treatment of many nerve affections, massage is almost indispensable. The superficial location of the peripheral nerves and their relation to the muscle tissue, making them easy of access, and the influence of mechanical measures upon the peripheral reflex arc of the sympathetic nervous system, afford a very broad application of the art to nervous diseases.

Massage is adapted to exert a stimulating and sedative effect upon the nerve, according to the method of application. The Pflueger-Arndt law of nerve excitability refers to normal nerve tissue, and is as follows: "Weak stimuli excite the activity of the nerve; moderately strong promote it; strong retard it; the strongest abolish it." The degree of stimulation should be proportionate to the sensitiveness of the nerve; weak pressure on a hyperexcitable nerve may call forth a response equal to the strongest stimulation of a normal nerve, and strong excitation may have little or no effect upon a hyposensitive nerve. Bearing in mind these physiological laws, it is not difficult to prescribe for a nerve condition according to the effect desired. Bum sums up these facts in a few words: "Vibration and percussion produce an irritative effect, capable of being regulated, upon the voluntary and involuntary muscles and upon the nerves. This causes, according to its intensity, an increase or decrease of the condition of excitation. The irritating action does not seem to

Fig. 27.—Exercise 14.

Fig. 28.—Exercise 15.

Fig. 29.—Exercise 15.

Fig. 30.—Exercise 16.

Fig. 31.—Exercise 18.

Fig. 32.—Exercise 19.

be confined only to the peripheral filaments and the stems of sensory, motor, and mixed nerves, but seems also to influence the nerves of secretion and to cause excitation of the vasomotor nerves."

Beside the direct action upon the nerve structure, the latter may be further influenced by mechanical manipulation—active and passive movements which have for their object the stretching of the nerve, thereby breaking up adhesions, and, according to Zederbaum, acting in the same manner as pressure on the nerve. Further than this, the massage and passive movements serve to strengthen the affected muscles.

Winternitz attributes the neuralgias to the accumulation of the products of fatigue in the nerve, and credits the action of massage and its allies to their influence upon the vasomotor nerves, by means of which a more active circulation is promoted and the waste products eliminated.

Neuralgias.—The occurrence of *neuralgias* and *neuritides* as local expressions of constitutional disease is so nearly the rule that prompt and permanent results cannot be expected unless appropriate measures are directed against the primal cause. Rheumatism, gout, alcoholism, diabetes, toxic states, pressure from tumor growths, or bone disease (particularly of the spine), displaced structures, as fractures or exudates, adjacent congestion, as in the pelvic organs, tabes, and diseases of central spinal origin must each receive its appropriate treatment. Massage can do no more than to offer valuable assistance in the treatment of many of these cases.

The *occipital neuralgias* are characterized objectively by tenderness of the nerve trunks included in this region. There are three principal *tender points:* first, that of the great occipital nerve which makes its exit midway between the mastoid process and the spinous process of the upper cervical vertebra; second, that of the cervical plexus which lies somewhat above the middle of the neck, between the trapezius and the sternomastoid muscles; and, third, that of the small occipital and great auricular nerves which lie directly behind the mastoid process.

Vibration gives, perhaps, the greatest relief, and may be either manual or mechanical. Tapping, compression, and friction should follow this procedure. Musical vibration has been employed upon the theory of Granville, that "pain is due to disharmony."

Brachial neuralgia (neuritis) offers direct contact in the axilla, and to the individual nerves, where they lie most superficial. Vibration, tapping, and stroking are all indicated.

Intercostal neuralgia may only be expected to yield to massage when such conditions as tabes, root or meningeal inflammation, spinal tumor, or nerve compression (scoliosis, etc.), pleurisy, and pulmonary tuberculosis, aortic aneurysm, etc., have been ruled out. The *tender points* are three: one, situated just laterally to the spinous process where the nerve exits from the intervertebral foramen; two, in the middle of the inter-

costal space where the perforating lateral branch runs just under the surface; and, three, near the sternum or just lateral to the middle of the abdomen where the anterior ramus perforates the muscles. Rheumatic and gouty neuralgias may show excellent results from massage properly applied to these points. General massage of these regions may be added. Such measures also apply to other regions affected, *facial, crural, sciatic,* etc.

It is a very common occurrence for the first treatment to call forth an attack of pain, but this should not persuade the physician to abandon the treatment, for usually the operator, by continuing the treatment, sees the attack disappear under his hands.

Sciatica.—For the treatment of the sciatic nerve by means of massage the most successful manipulations are deep kneading, as practiced by Zabludowski and Metzger, together with strong pressure on the nerve and stretching exercises; simple friction and vibration; completing the treatment with general massage of the musculature; exercises of the lower extremity and trunk are sometimes added. Deep kneading offers great benefit by stimulating the circulation, flushing the part, as it were, with a fresh supply of pure blood, increasing its elimination, and aiding its renovation. Percussion still further favors these effects. The severer measures are employed with good success in many cases, such as applying the strongest possible pressure, by means of the reinforced thumb, upon the nerve at its exit.

Negro advocates energetic pressure on the nerve at its point of exit from the foramen, repeated after an interval of a few minutes. Patient remains free from pain from a few hours to an entire day. He cites as cured 100 out of 113 cases treated by this method. Average number of treatments was 6, given on alternate days. We wish to urge great care in the execution of such measures; paralysis has resulted at times.

These procedures may be carried out in the following manner: the patient lies on his abdomen and relaxes as far as possible his lower extremities; the operator begins with heavy friction (stroking with the flat of the hand) from the heel to the lumbar region, and in such a way that the hands follow each other in rapid succession. The painful points receive special attention; they are rubbed, vibrated, and pressed. The stroking and kneading are applied all along the course of the nerve by means of the thumbs, which press in between the muscles which border it throughout its course. Strong kneading of the calf and thigh muscles completes this portion of the treatment; the patient turns upon his back, and, after general and vigorous massage of the extensor muscles of the leg, the operator may proceed to move the limb passively, only slightly stretching the nerve at first, but gradually increasing with each succeeding treatment, according to the reaction of the patient.

Exercises at a later stage further increase the efficiency of the treat-

ment. These consist in active and passive stretching of the nerve and preparing of the limb for its normal functions. The patient, in the standing position, abducts the affected leg while standing on the other leg. He performs a circle with the affected leg, rotating it at the hip. With the feet together, he bends the body forward. With the feet together, he assumes the squatting position.

Brieger advocates warm baths (36-38° C., 96.8-100.4° F.), in which passive and active movements of the leg are carried out. There are various methods for stretching the nerve, and their severity is increased from day to day. The duration of the treatment is up to half an hour, according to the condition of the patient. Massage may be added, and is said to possess a remarkable efficiency at such a time.

Headache.—Massage is successfully applied to the headaches of *anemia,* those resulting from *loss of sleep,* those dependent upon *gastro-intestinal disorders,* as constipation (abdominal massage and manipulation being included), the habitual headache so common in *neurasthenic states,* those conditions—nervous, muscular, and vascular—the description of which varies largely with the individual, but which are usually described by the patient as drawing sensations; dull, heavy ache; lameness; congestion at the back of the neck, etc.; there is frequently a desire to stretch the muscles, or to press them, and examination shows varying degrees of tenderness of a diffuse nature, often some local heat, and a certain rigidity. Careful examination of the neck and head muscles in this last condition described often discloses the presence of muscle nodules of induration. Attention was long ago called to these nodules by the Swedish writers, and the Swedish masseur will often be the first to discover them. They appear as rather firm, rounded nodules, which may be rolled under the finger, and are exquisitely tender. They are not confined to the head and neck, but may appear elsewhere on the body—the back muscles in lumbago, the shoulder muscles, the thighs, etc. If cut down upon, as the author saw done in one case, no trace of the nodule is to be found; it is probably a muscle infiltration of vasomotor origin. From time to time attention has been called to this condition, and of late it has been emphasized by Edinger and Auerbach, most recently by Mueller. Edinger goes so far as to say that massage is the only cure for such conditions. Such headaches are usually the expression of toxic states, and represent forms of myositis and vasomotor spasm. Massage gives temporary relief to *migraine,* which is a gouty or rheumatic manifestation, also to those toxic headaches resulting from nicotin, alcohol, and lead poisoning. It influences favorably headaches due, reflexly, to disordered states elsewhere in the body—as the pelvic organs, enlarged prostate—to which the masseur may also have his attention directed.

The application of massage to these individual cases varies somewhat according to the cause. A general massage of the head is indicated in

all of these conditions, and this consists in a series of manual movements intended to renew the blood supply and to relieve the tension which is so often present. Stroking and friction, kneading, and rolling of the scalp are systematically carried out; the head is grasped between the hands and the scalp moved in a circular fashion; chucking; vibration of a mild type is especially soothing, also firm pressure. Should the headache be due to congestion of the brain, depleting measures are indicated, stripping the vessels of the neck, hastening the flow of blood and lymph away from the cerebral cavity. Breathing and posture influence the circulatory flow, and for this reason the downward strokes are advised to be made at the same time as inspiration. Hoeffinger, Gerster, Kellogg, and others have advocated special methods—some from behind, and others from in front—but we think, with Kellogg, that the treatment of the posterior neck muscles is a very important part. In the condition described as "muscle nodules" the massage should be of a very firm and positive type; rubbing, stroking, and vibration, but particularly the former, are applicable. A circular rubbing and stroking in the direction of the lymph vessels are most effective.

Naegeli has methods of his own invention by which he stretches and manipulates the neck so as to produce favorable results in cases of headache. Upon this theory of stretching the affected nerve and its surrounding tissues, he develops a whole system of manual manipulation which, when skilfully applied, may give prompt relief to painful conditions in almost any region of the body.

Occupation Neuroses.—The *treatment* of writer's cramp consists in writing exercises carried out before the physician, and this is preceded or followed by vigorous massage of the entire extremity. Firm friction, deep kneading, and light percussion especially are recommended; all the muscles of the hand, the tendon sheaths, the forearm—where more or less spastic, tender areas may be found—the upper arm, shoulder, and even the trunk may be included. Exercises, passive, active, and resistive, may be necessary in the severer forms. In these exercises the fingers are moved in all possible directions, the wrist, the elbow, and the shoulder are systematically manipulated. The movements should be rhythmically executed, synchronously by both upper extremities or alternating on the two sides; their complexity and severity are gradually increased. The patient should practice these at home several times daily. It is also well to recommend to the patient some form of mechanical occupation, such as carving, rowing, book-binding, piano-playing, sewing, knitting, etc.

The neurasthenic element in these cases must always be considered; the patient needs much encouragement, precise instructions as to the execution of all exercises, a thorough understanding of the duration of the treatment, which usually lasts over some weeks or months, according

to the severity of the case. The "rheumatic element," if present, needs attention, and the general physical condition, for those affected are often anemic, easily fatigued individuals who need correction of their entire mode of living. The simpler and more direct the treatment the better and surer are the results. The tendency to relapse must always be borne in mind.

The musician's cramp occurs among pianists, violinists, and other stringed instrument players. The mechanical treatment for these conditions is absolute rest and light massage at first—friction and kneading especially. The whole upper extremity should be included. Exercises, mostly in the large joints—shoulder, elbow, wrist—are recommended.

Bum relates curative results with a large majority of cases, including those suffering from writer's cramp, piano, violin, zither, and cello players, as well as dancers, bicyclists, tennis players. The treatment covered a period of three weeks to four months.

Atrophy.—It seems wise to include under this general symptomatic term those diseases which present muscle atrophy of whatever description or from whatever cause. Whether the atrophy is due to a neuritis or to an anterior poliomyelitis, that is, whatever portion of the peripheral motor neuron is attacked, the indications for the treatment of the affected muscles are the same, namely, nutritional.

It is not difficult, then, to enumerate the diseases of this segment of the motor tract apparatus; these are regional, as facial palsy; brachial neuritis; birth palsy; pressure paralysis, most frequently of the forearm (musculospiral); the peroneal paralyses, etc.; or general, as toxic polyneuritis, due to alcohol, lead, toxins of infectious diseases, etc.; and finally diseases of the spinal motor cells, chief among which are anterior poliomyelitis, progressive muscular atrophy, syringomyelia, etc. There are also the atrophies of primary myopathy, and of disuse.

With recent conditions, a week or more should be allowed before anything but the lightest massage is applied. The more chronic conditions of muscle wasting afford ample evidence of the beneficial effects of massage, either in hastening the recovery (neuritis of various origins), improving the condition (anterior poliomyelitis), often to a surprising extent, or retarding the progress of or even improving such a disease as progressive muscular atrophy.

Following the paralysis of one group of muscles, contraction of the antagonistic group frequently occurs, and this is especially the case the more severe the paralysis and the longer its duration. Firm adhesions may form so that the joint becomes markedly deformed. The first indication is to break up these adhesions by massage, passive movements, and traction. Permanent support should then be afforded the joint by means of the splint or other mechanical measures which prevent the joint from resuming the abnormal position. These appliances are often

a test of the ingenuity of the physician. And when the normal motion is regained, attention must be constantly directed toward the prevention of any recurrence of the faulty condition.

The massage in these atrophic conditions should consist in those movements which stimulate nutrition, through the circulation; the effects of muscle inactivity are more or less overcome by this means. Centripetal friction, deep kneading with all its modifications, circular kneading, and percussion are most useful.

Spasticity.—This condition of muscle spasm, which is a result of central or spinal irritation of the primary motor neuron, is relieved, and the contractions resulting from long-continued muscle spasm are overcome, to a large extent, by massage. Such spastic conditions occur in cerebral lesions affecting the motor areas, or its cerebral and spinal tracts. Among the most frequent of such conditions are cerebral hemorrhage or thrombosis; multiple sclerosis; cerebrospinal lues; specific spinal paralysis; compression of the cord from whatever cause, tumor, Pott's disease, dislocation. The patient may often be temporarily relieved and often materially benefited by relaxing massage, combined with passive and active movements; the pains from muscle cramps are alleviated, and the secondary atrophy consequent to long disuse is counteracted. The degree of recovery can only be fully demonstrated after making use of every means to bring the affected part to as nearly as possible a normal state of nutrition and relaxation. For this reason it is essential to continue the treatment for some weeks, with regularity and perseverance.

The passive movements should include each affected joint, and should be carried out to the full extent of physiological movement. Where adhesions exist, these must be gradually broken up by firm and persistent force, and it is for this reason often advantageous to exert more or less constant traction upon the spastic muscles by means of splints or mechanical apparatus.

The active movements are particularly applicable in those cases of long duration where the part has fallen into disuse, and where, by reeducating the voluntary control and stimulating the voluntary muscle groups, very favorable results may often be obtained. The reluctance of the patient to use a part which he can only awkwardly control, and which, therefore, has added to its already injured condition that of disuse, must be insistently guarded against, and the patient should be urged to use the part in as nearly a normal capacity as possible. Examples of a few active exercises are here given, and these should be modified to the individual case, according to the region affected:

Finger Movements.—Flexing and extending the fingers and thumb, both simultaneously and separately; ab- and adducting the fingers, both simultaneously and separately; flexing and extending the fingers in the first and second phalangeal joints; rotating the fingers separately; touch-

ing the tip of each finger to the tip of the thumb; touching the tips or sides of alternate fingers, etc. The normal movements of wrist, elbow, and shoulder may be executed voluntarily.

Lower Extremity.—Flexing and extending the toes without participation of the ankle joint; movements of the ankle, knee, and hip joints, in all directions; in the sitting or standing position, with the heel raised, tapping the toes on the floor, flexing the ankle to the full extent each time, etc. Later more complicated exercises may be introduced. It is often of advantage in one-sided paresis that the patient either imitate the movements as demonstrated by the operator, or that he carry out movements of the affected side in unison with those of the normal side. Frequent practice and exactitude of execution are essential.

It should also be borne in mind that appropriate measures for the prevention of contractures should be commenced at an early date, as these present much greater difficulties after they have once formed. It is sometimes impossible to prevent them, however.

Tabes.—Symptomatically, massage has its place in the palliative treatment of tabes dorsalis. It relieves the hypotonia and the feeling of "stiffness" which the patient often describes, and which is an instinctive, more or less voluntary condition which adds to his security by heightening his joint sensibility; it favorably influences the muscle pareses, and may relieve the pains. Defective circulation so frequently goes hand in hand with tabes, arterio- and cardiosclerosis, and the sensory trophic nerves are so universally involved, that nutritional disturbances of a local or general character are sure to develop at some period of the disease; massage, general and passive movements, are well employed here; and also massage of the back for any effect which it may produce upon the spinal nutrition. Massage, particularly vibration, over the bladder is recommended in vesical disturbances, and abdominal massage in combating the frequent, obstinate constipation (see Constipation).

Reëducational Movements in Ataxia.—Even before the pathology of tabes was understood, gymnastic movements were employed in this disease by the Swedes, and, it is said, not without success. But, when the nature of the lesion became known and the manner of its working was established, motor training for ataxic muscles acquired many advocates who developed more or less individual but similar systems of training based upon the same principles, namely, the possibility of compensation for the defective sensibility by educating to as high a degree as possible the sensibility which remains.

It was Frenkel of Heiden, Switzerland, who formulated, upon the theories of v. Leyden and Goldscheider, a simple and practical system for the reëducation of the ataxic motor apparatus. He especially emphasized as the essential part the frequent repetition of the movement and the care and exactitude with which it is carried out. Thus the

system becomes a trainer of those forms of deep and to a certain extent superficial sensibility which inform us of the relation of the different parts of our bodies to one another, and of their positions in space. In the process of training these sensibilities the sense of vision is, at first, made to play an important part.

Upon the theory that this sense of "position" could be sufficiently restored to the tabetic to enable him once more to direct his movements—coördinate them—his motor apparatus being adequate, it was necessary to develop exercises which would permit of practice in the finest coordination, in the greatest accuracy of execution, and which possessed such simplicity and ease of execution that the easily fatigued muscles of the tabetic would not suffer injury.

The patient is first examined as to his degree of ataxia—whether he is able to walk alone or supported—whether he can perform simple movements accurately; to what extent his nervousness influences his movements; also as to his hypotonia and the presence of trophic disturbances, both of which materially influence the prognosis for the worse. A careful sensory examination, particularly of the deep sensibilities (muscle and joint sense, position) will give one precise information as to the impairment of function.

The exercises are graded from the simplest to the most complicated, and may therefore be applied to any degree of ataxia. Those for the lower extremities are performed either in the lying, sitting, or standing position. The first are most easily performed, since they eliminate the weight of the body and its balance; the legs may even be supported by the doctor or by a suitable apparatus. The patient, lying on a couch with his head and shoulders raised, so that he may watch every movement, flexes and extends one lower extremity, the heel resting upon the couch and sliding with a smooth continuity in a direct line, not with a jerky, interrupted movement; slowly and exactly, and not in a hasty fashion, a tendency of almost all tabetics. In the same manner similar exercises are performed, including the physiological range of movement; flexion of the leg, abducting and adducting, extension; voluntary halts are made or called by the doctor, etc. The same exercises are performed with both legs simultaneously. Only when these have acquired a certain proficiency should other exercises be added. The same exercises are performed with the heel a few inches in the air; the heel is brought to rest upon a point indicated on the other leg. The heel is run along the anterior border of the tibia from the ankle to the patella; halts are made at regular intervals; the heel is moved from the tibia to the couch, up and back again, etc. Thus a number of combinations may be made, and the variety is appreciated by the patient, who should, on his part, exert every effort to concentrate his attention upon the exercise. Fatigue must be guarded against, and frequent periods of rest allowed. Practice for

five minutes several times a day is much preferable to longer periods less often. From the outline of the movements given above, others more complicated and extensive are evolved. Passive movements for the education of "muscle sense" have been advocated by Goldscheider. Here the patient, with closed eyes, concentrates upon the movements of his joints, endeavoring to perceive and define every peripheral sensation associated with this movement.

Special apparatus has been constructed to afford greater range of exercises; the heels are placed in hollows made at regular intervals in a board; a crossbar adjustable to varying heights is touched by the toes and the heels, etc. Goldscheider and others have elaborated many different sorts of apparatus, but, apart from a few pieces which we will mention later, they are entirely unnecessary. As soon as possible the patient is taught to get upon his feet from the *sitting posture;* this is the most important movement executed from this position. Here first begins a close analysis of movement in the erect position and its relation to gravity. The patient should have demonstrated to him the following points in the process of (1) "standing up," and (2) "sitting down."

1. Draw feet back until they are on a line with the edge of the chair; move somewhat forward on the chair; bend the body forward until the knees begin to extend, then extend the knees entirely and cause the body to assume the erect position.

2. In reverse order, the body is bent forward while the knees are flexed, thus keeping the line of gravity far enough forward to enable the body to be lowered slowly into the chair.

Care must be taken in both of these exercises lest the patient pitch forward. He may at first support himself on the arms of the chair, or by placing his hands on his thighs, but later he should let his arms hang at his side. It is often astonishing to see the ease with which this act is performed after these few points in mechanism are learned.

Exercises in the erect posture consist in standing on both legs, taking short steps forward, sideways, and backward, first with one foot and then with the other; rising on the toes; bending the knees; resting on one foot and toe of other, and on one foot alone; walking sideways, forward, backward, and turning; taking steps of various lengths; exercising on a wide base (heels 9-12 inches apart), and on a narrow base (heels 3 inches apart); various modifications of these exercises, such as walking with the knees slightly bent, walking zigzag, etc.; finally, walking up and down stairs, etc.

In order to perform some of these exercises lines and footprints may be painted upon strips of linoleum about twenty feet long. A square of linoleum on which are painted footprints to allow lateral, forward, backward, and oblique steps with each foot is very useful. A small platform on two opposite sides of which lead flights of three steps may easily be

constructed by any carpenter. This is all the apparatus which is actually required. In all these exercises the following points are to be carefully noted: The patient, at first, watches every movement which he makes; as he progresses he looks a few feet ahead of him, then straight ahead. The question of balance is a very important one; he is taught to shift his weight from one leg to the other, and at first he should do this before he moves the free leg; later he may shift his weight and move his leg at the same time in the normal manner. The proper training in this regard greatly facilitates his walking, and it is for this reason that the first exercises should be those best adapted to this purpose, namely, shifting the weight from one extremity to the other with a very slow, rocking motion, after having taken a step forward, sideways, or obliquely; balancing on one foot supported at first by the toe of the other, then without support, and finally flexing and extending the free extremity at the same time; and walking sideways. Above all, the exercises should be slowly and deliberately executed, and this is best obtained by insisting that the patient be certain of his balance before he attempts the movement. It is hardly possible to perform these movements too slowly. Ordinarily one leg is more severely affected than the other; special attention should be paid to this, and an effort be made to develop the two extremities equally, and to avoid the natural tendency to make more use of the better leg. Tabetic patients avoid balancing themselves upon their toes; in stepping forward and sideways, the toes should touch the floor first, and in taking measured steps the edge of the sole should touch the lines accurately. There is a strong tendency in the tabetic to turn the toes outward; this should be overcome. The danger of falling must be borne in mind and constantly guarded against. A patient's pulse is often the best indication of fatigue. Walking with slightly bent knees is an excellent exercise. Walking up and down stairs needs again special attention as to the center of gravity. By carefully observing the different stages, according to the rules already given, the mechanics of the act are not difficult to explain. It is wise to support those patients who are unable to stand by means of a broad belt, made of non-elastic material, and supplied with stout leather straps for fastening and two iron or wooden handles posteriorly. By means of these handles the "paralytic" patient may be supported with less danger than by the arms, especially if these are severely affected, as dislocation or fracture of the humerus may occur. Very loose joints may be supported by bandages. Electricity and massage, resistance movements especially, are strongly advocated for the hypotonic musculature.

The exercises for the upper extremity consist in simple coördinated movements, such as flexion and extension at the various joints, executed slowly and smoothly; the joints of the hand should receive special attention, and the fingers should be taught to move separately and to-

gether. These exercises require a certain amount of apparatus, which is easily available—pencil and paper on which the patient traces or draws straight and curved lines, or he may follow a groove in a board, holding the pencil lightly, maintaining the same pressure and slow rate of movement throughout. This should be a free arm movement, and may be varied by altering the position of the board. Double grooves may be made, thus allowing both arms to practice at the same time. On the other side of this board may be pasted, at regular intervals, paper discs the size of the finger tips.

Discs of paper may be pasted, or small circles the size of the finger tips may be painted, at regular intervals upon a board about one foot square. These discs are numbered, and the patient requested to place his finger, with free arm movement, upon the disc bearing the number called by the doctor. A similar board, or the same one, may have holes into which the patient inserts pegs or large pins. A cribbage board is an excellent example. When cards are added, the patient will find diversion as well. Solitaire may be played, carefully, with exact placing of each card. Checkers or dominoes, made into piles or designs, afford a useful diversion. Various designs with straight and curved lines may be retraced. Finally, writing with pencil and pen is added. The patient should make every effort to employ his hands in as many ways as possible; in dressing himself, in helping himself at table; he may play the piano or some other musical instrument. Thus he practices several times each day with exactitude and patience, at first before the physician, and later, if he shows aptitude, by himself.

Contraindications to these exercises, especially as pertains to the severer ones for the lower extremities, are self-evident—general weakness, uncompensated organic disease, trophic joint disease, and blindness. A fair degree of intelligence is required.

The foregoing exercises apply not only to locomotor ataxia, but permit of modifications in their application to other types of incoördination. Goldscheider recommends such practice of reëducation therapy in *intention tremor* and *athetoid movements,* which, he says, may be somewhat benefited. It has been recommended in long-standing cases of *chorea,* and systematic movements have shown improvement in *hysterical contractures* and in *tics.* *Writer's cramp* has already been referred to under occupation neuroses. Zabludowski reports a case of *Friedreich's ataxia* improved by massage.

Since the time of Charcot vibration has been used to relieve the tremor of *paralysis agitans,* and it offers temporary relief in some cases. Massage of the stiffened muscles is well added.

Neurasthenia.—Under this vague term we group a multitude of primary conditions which present the symptoms of diminished nervous energy. Massage naturally suggests itself and often proves of value in

the restoration of these fatigue processes, with their consequent nutritional disturbances.

Daily calisthenics, practiced on rising and on retiring, for five or ten minutes, and combined with deep breathing, give a splendid feeling of well-being to some patients. Such exercises are noted under the head of "Diseases of the Respiratory System," also under "Constipation," and we here add a list which offers further suggestions. (See also Vol. IV, Sec. IV, Chapter XXI.)

1. Stand erect, let arms hang down relaxed beside body, clench hands, and touch shoulders alternately with fists.

2. Touch shoulders with both fists at same time.

3. Stand erect, extend arms sideways same height with shoulders, bend arms from elbows, and touch shoulders alternately.

4. Touch both shoulders at same time.

5. Stand erect with hands on hips, bend body backward and forward.

6. Same position as 5. Bend body sideways from right to left (exercises 5 and 6 should be done slowly to avoid dizziness).

7. Take attitude of a boxer. Step forward with right foot as far as possible, and push arm with clenched fist forward as hard as possible. Arm and foot motion should be uniform.

8. Repeat exercise 7 with left foot and left arm.

9. Repeat exercises 7 and 8 with right and left side alternately.

10. Lie flat on floor on back with hands underneath head, raise extended legs alternately at right angles with body.

11. Same position as exercise 10. Raise both legs at right angles with body.

12. Place arms with clenched hands on chest, remain flat on back, keep body rigid, push arms forward, trying to sit up at same time.

13. Lie flat on stomach. Extend arms in front of head, raise arms and legs from floor at same time (be sure to raise knees and elbows from floor).

14. Flat on back. Place hands with palms flat on floor beside body, hands should be in same line with hips and at a distance of about 15 inches from body to secure balance. Throw both legs over head and try to touch floor with toes.

Do each standing exercise about 8 times, each floor exercise 5 times in beginning, and increase exercise according to increase of strength. Dress lightly when exercising with plenty of fresh air in room.

The patient should resist, to some extent, his own movements. Pride and enthusiasm in execution should be fostered. He should be cautioned not to exercise for at least two hours after a meal, and if he complains of faintness to take a few sips of milk, coffee, or tea.

These exercises may also be practiced during the day, when they may

take the form of a diversion. Dumbbells may be used, or pulley weights. Horseback riding, boxing, fencing, dancing, golfing, rowing, swimming, and such sports combine recreation of a more varied type, and offer greater attractions to the fastidious. Manual labor of all kinds is strongly advocated, wood-chopping, gardening, carpentry, etc. Whatever work is to be done, whatever exercise performed, the purpose should be emphasized, and exact instructions given.

The sexual neurasthenic is usually greatly benefited by taking up some form of vigorous exercise. Massage of the prostate may be indicated.

To the foregoing procedures may be added spinal vibration, such as may be given by current hand vibrators, and general tonifying measures, such as hydrotherapy offers.

Massage may be employed in hysterical conditions, or rather upon those who show hysterical stigmata along with functional organic disorders; malnutrition, anemia, and the symptoms already noted under neurasthenia. It may be possible to favorably influence the anesthesias and hyperesthesias by massage in combination with suggestion, but it is often wise rather to direct the patient's attention away from these manifestations.

Through the influence of massage upon the nutrition and metabolic processes, toxic *psychoses,* in which exhaustion, depression, and even stupor are present, show improvement. Bum, quoting Maggiorani, gives as *contraindications* all forms of mania—with the exception of the hysterical—melancholia with anxiety or agitation, epileptic psychoses, as well as those patients afflicted with acoustic hallucinations.

Certainly massage is contraindicated in all forms of mental disturbance in which it is demonstrated, after a few treatments, that it aggravates rather than pacifies the patient's mental condition. Here again the tactfulness of the operator may be the determining factor.

Gastrointestinal Diseases

In all cases of gastrointestinal disorder of a chronic nature, disturbed nutrition and more or less toxemia follow as natural accompaniments; whether these disorders are due to digestive disturbance of a functional type, to alteration of the digestive juices—gastric, hepatic, pancreatic, enteric—to ulcer formation—or due, secondarily, to circulatory disturbance, reflex pelvic or glandular aberration—general massage is frequently useful in combating the toxemia and in overcoming the ill effects of the prolonged rest so often required. It should be prescribed only upon definite indications. If the patient exercise sufficiently to facilitate elimination; if his peripheral circulation is overactive, as in hyperthyroid conditions, massage is usually not indicated; but if, on the other hand,

there is a sluggish, atonic state, if exercise is limited, and elimination poor; above all, if rest and every means of saving the expenditure of energy are imperative, general massage may exert a very favorable influence. In such cases abdominal massage, unless contraindicated, should be included in the treatment, and the abdomen should receive special attention where chronic constipation and splanchnoptosis exist.

Chronic Constipation.—It is certain that a very appreciable number of patients suffering from chronic constipation present the features of an atonic abdominal wall, and more or less prolapse and atony of the abdominal contents. There is general retardation of function, both motor and secretory, through diminished activity; there are accumulation of material, fermentation, dilatation, passive congestion of the portal system, and frequently distressing visceral sensations—dragging pains elsewhere in the body from faulty posture, or toxemia, etc. The prime indication for abdominal massage is atony, and it has been authoritatively stated that the permanent cures of chronic constipation have been brought about by treating this causal factor, which is to be sought not only in the "atrophy and insufficiency of the muscular elements of the intestine, but also of the abdominal wall" (Bum).

Kellogg gives the following rules which are to be observed in abdominal massage:

"1. General abdominal massage should not be administered until two hours after eating.

"2. The bladder should always be emptied just before abdominal massage.

"3. In obstinate cases of fecal accumulation a coloclyster (large enema taken in right Sims's, or knee-chest, position) of warm water should be administered, the water being allowed to pass off before treatment.

"4. The patient should be taught to relax the abdominal muscles, and to breathe deeply and regularly during treatment.

"5. If the abdomen is very sensitive, apply a hot fermentation before giving the massage.

"6. If the skin perspires very freely, render it firm and smooth by sponging with cold water.

"7. Very 'ticklish' patients require careful education by avoidance at first of superficial movements.

"8. Pain and coldness of the extremities, or depression, after abdominal massage, are due either to bungling or violent treatment, or to extreme hyperesthesia of the abdominal sympathetic. In such cases employ fomentations and the moist abdominal bandage in connection with massage.

"9. It is important in all manipulations of the abdomen to exercise great care not to excite pain. All movements should be executed in such

a manner as to avoid sudden thrusts, thereby causing the patient pain or other disagreeable sensations, as such disturbances create rigidity of the abdominal muscles, thus seriously interfering with the effects of the manipulations.

"10. In applying massage to the abdomen, the operator should stand over the patient, so as to aid his hands, as far as possible, by the weight of his body, taking care, of course, to graduate the pressure to the requirements of each individual case.

"11. All deep-kneading movements in massage of the abdomen should be slower than for other parts of the body, to allow time for movement of the fecal mass."

The methods employed are circular stroking, at first very lightly, to overcome the reflex muscle spasm. Here the palmar surface of the hand is placed flat upon the abdomen in the region of the umbilicus; the fingers point to the right beneath the costal borders, and lightly stroke from right to left, the wrist being used as a pivot. Vertical stroking may follow if the patient's abdomen is not too sensitive ("ticklish"). Compression of the solar plexus and lumbar ganglia as a means of stimulation has been advocated, but this should be executed only with great care, and, we believe, should be avoided altogether when hypersensibility exists; it is frequently a sign of spastic constipation, to which we have already alluded. Kneading of the abdominal muscles, and deep kneading of the abdominal contents, digital, palmar, and with the fist, are excellent measures—small circles may be described by the tips of the fingers, one hand being reinforced by the other laid upon it; the course of the colon is followed. And it should be borne in mind that too severe excitation may lead to undesirable spasm, or even relaxation of the intestinal wall, as well as the ill effects of trauma. Vibration is applied by means of the flat of the hand, by the fist, and by the finger tips with firm pressure. Percussion consists in the usual methods as applied elsewhere upon the body. These last two procedures are especially advocated by some authorities.

Unless the physical condition of the patient forbids, abdominal massage for abdominal atony is usually combined with special exercises to develop the abdominal musculature by voluntary effort. A list of the most serviceable exercises follows.

Bending the body forward and backward, and rotating the trunk upon the hips—this last may be carried out in the standing or sitting posture. Hanging from a bar, the extended lower extremities are flexed in midair upon the trunk, or, the same movement, lying upon the back, the limbs are raised into the air, or, the feet made fast by straps or a heavy weight, the trunk is raised to the erect position, and rotated. These movements may be executed with or without resistance. General gymnastic exercise and outdoor sports may be recommended.

Breathing exercises may be advantageously combined with some of these movements, and deep breathing is to be recommended for its beneficial effect upon posture, for its circulatory effect, and for any action which it may directly have upon the liver and other abdominal viscera. It may be necessary or advisable to employ an abdominal belt or support. Electricity in the form of faradism and galvanism is useful at times.

At the initial stage of the treatment it is wise to make use of a good tonifying cathartic in diminishing doses; enemata or irrigations may be necessary. Gradually a normal equilibrium should be established. The duration of such treatment practiced daily varies from four to eight weeks.

Disorders of Metabolism

Obesity.—It is doubtful if massage alone is of any value whatsoever in reducing fat. When given together with systematic exercises, and the other above-mentioned methods, it undoubtedly affords a valuable adjunct. In the beginning the exercises prescribed should be very mild ones, consisting chiefly of regulated walks in the open air. If there appears no contraindication the amount of daily exercise can rapidly be increased. The individual must be made to see the necessity for active outdoor exercises. Where practical, he should be interested in golf, tennis, and horseback riding. Such diversions as these, together with scheduled walking excursions, usually appeal more strongly to the patient than gymnastic exercises. At first the walking should be done on level ground, and later, as the patient becomes accustomed to it, hill-climbing should be taken up. These are the Oertel exercises, and are of the greatest value.

The gymnastic exercises employed consist of movements which will strengthen the abdominal and back muscles, and breathing exercises.

1. With the hands clasped behind the neck, the body is bent forward, backward, and from side to side, and then rotated at the waist. This should be repeated in every direction eight or ten times, slowly and evenly, and with the lungs alternately filling and exhaling.

2. With the hands held high above the head, the patient lying supine, the trunk is slowly raised as far as possible, while the hips and lower extremities are held as immobile as possible.

3. In addition to the above, simple calisthenic exercises, as are described on pages 306 and 321, should be practiced.

It must be borne in mind that none of these methods will prove of much value if employed alone. One is essential for the success of the other, this being particularly true of dieting and exercising.

Gout.—Inasmuch as obesity is frequently a forerunner of gout, a great deal may be done in the way of preventing it by employing those measures described above for the relief of the former. The two con-

ditions are very often found together, and, since they both represent a metabolic disorder which results from overnutrition and faulty elimination, the treatment of gout by exercises is practically the same as for obesity. In gout, however, it is seldom necessary to employ as strenuous exercise as in obesity. The individual's life must be properly regulated, and all avenues of elimination kept active. This, of course, involves the taking of the proper amount of exercise. Gouty deposits around the joints are often treated by massage, and usually successfully, provided the manipulations are very gentle in the beginning, gradually increasing a little at each treatment.

Rheumatism.—In the treatment of rheumatic conditions massage and passive movements occupy a much larger field of usefulness than gymnastics. Well-regulated exercises, however, may be successfully employed as a preventive measure in those individuals possessing the rheumatic or gouty diathesis.

In acute inflammatory conditions of the joints massage must be employed with the greatest care. It should not be undertaken at all unless one is fortunate enough to secure the services of an expert operator, for it is a simple matter to do a great deal more harm than good by carelessness and ignorance. Needless to say that a hot, swollen joint must be put at absolute rest. Any manipulation of the joint whatsoever would not only cause unbearable pain, but would aggravate the condition. If, however, we gently massage the limb above and below the joint, and employ the more vigorous methods to other parts of the body remote from the site of the inflammation, we are able to encourage drainage from the affected part by dilating the peripheral vessels, and to relieve the heart of some of its burden. Oxidation and radiation are both promoted, two factors of great value in any febrile affection. It is in the neighborhood of the joint that the greatest care must be exercised. The operator's hands must not come too close to the inflamed part. Stroking, friction, and very gentle kneading are the methods of procedure to be employed here, while in the more remote parts of the body all of the methods ordinarily used are indicated. As soon as the pain, swelling, and fever have sufficiently subsided, very gentle passive movements of the joints are indicated.

When some part of the muscular apparatus is attacked, as in lumbago or torticollis, the treatment by massage should be similar to that just outlined above for the parts surrounding an inflamed joint. With subsidence of the pain, more vigorous methods may be employed.

In subacute and chronic rheumatism massage and passive movements of the joints afford ready relief, and when employed systematically we are able to keep the musculature and joints in a more flexible and healthy condition. In chronic rheumatism the joints particularly need careful attention. Passive and active movements, up to the limit of pain tol-

crance, practiced regularly every day, will do a great deal to prevent ankylosis. As we all know, there is a marked tendency, with individuals suffering from this disorder, to remain quiet and to take just as little exercise as possible. Needless to say, a sedentary life only aggravates the condition and encourages gouty difficulties in addition. The pain provoked when these individuals attempt to move about is often very intense, and they come to dread the slightest exertion. Hence, when massage is administered by a skilful operator, we have an excellent substitute for exercise. When properly given the treatments should cause very little, if any, discomfort.

In this, as in the other metabolic disorders treated above, one cannot hope to rely upon this method alone. Dieting, hydrotherapy, and drugs all have their important places in the treatment.

Arthritis Deformans.—Arthritis deformans is a condition which, in view of our present knowledge, is almost entirely dependent upon massage and manipulations of the joints for temporary relief. When these are employed early in the course of the disease they will, to some extent, retard the progress of the deformity. General bodily massage should be given in all cases, with special attention paid to the joints and muscles involved. It is essential that the treatments be given over a long period of time, and at a regular stated hour each day. The degree of force employed to overcome the ankylosed joints should depend upon the amount of pain provoked and its duration. If the pain only lasts for a few minutes, or for an hour or so, the same, or a slightly greater, degree of force may be used at the subsequent treatment. The muscles between the joints, particularly in the hands, must be vigorously and faithfully kneaded. A great deal can be done in this way to prevent atrophy of these parts. The patient must be encouraged to use the hands as much as possible. For this he must be taught to perform certain movements of the hands and fingers each day, movements that will prevent as far as possible stiffening of the joints, and such exercises as would help him to retain as long as possible the use of the hands for their proper function. For instance, he should be made to depend upon his own efforts to dress and to undress himself, etc.

Diabetes.—Massage and exercise are both of great value in the treatment of diabetes mellitus. The former should be employed in all cases, the latter in those individuals who are strong enough to be up and out of doors. Since we know that the muscles are the great heat producers of the body, it follows that massage and exercise, through their effects upon the circulation and tissue change in these parts, enable them to increase their activity in the combustion of glycogen.

Massage should be given regularly each day, beginning with half-hour treatments, and increasing to an hour or an hour and a quarter. Deep kneading and percussion are the methods that are of the greatest value.

In the absence of contraindications, the patient should also be made to take some simple form of exercise in the open air.

Sprains, Fractures, and Post-operative Treatments

Excellent results may be accomplished in the treatment of sprained joints by massage, but a great deal of skill and experience on the part of the operator is necessary. Here, as in treating acute rheumatic joints, more harm than good will be done unless the proper care and skill are exercised. For the first 24 hours after the sprain the joint must be elevated and at absolute rest. Cold applications should be constantly applied. After 24 hours the treatment should consist of gentle stroking, friction, and kneading of the soft parts about the joint. Two treatments a day should be given, and at each one the operator gradually comes closer and closer to the inflamed part, until after the second or third day, depending upon the severity of the injury, careful joint movements may be executed, and the tissue over the joint gently picked up and kneaded. It is chiefly in giving the passive joint movements that caution must be exercised, for any overextension or flexion will further injure the ligaments and tendons. As the swelling and tenderness disappear, the manipulations may be more vigorous, and the length of time devoted for each treatment lengthened. After five or six days only one treatment a day is necessary.

In the *treatment* of fractures massage should not be employed until after the broken bone has been reduced and immobilized in the usual manner for three days. After this the splint should be removed each day and gentle massage given to the entire limb, due care being exercised to avoid displacement of the ends of the bone. After a few days the length and vigorousness of the treatment should be increased. Should the immobilization apparatus prevent the free movement of any joint in the neighborhood of the fracture, care must be taken that it does not become stiff. At each treatment the joints should be freely moved, at first by the operator and later by the patient. Fractures involving the joints themselves require great care and attention. The active and passive movements in such cases must, of course, be guardedly given. The neighboring ligaments in such cases are very liable to become matted in the contracting cicatricial tissue, and their free movement interfered with. In skilful hands, however, this may easily be avoided, and the joint restored to its normal flexibility.

Massage has proven of great value in overcoming the deformities resulting for cicatricial contractures in certain post-traumatic conditions, and in preventing the formation of adhesions after operations upon nerves and tendons. Even though the wound heals by primary union, there is usually more or less matting together of the tissues. After a severed

nerve has been united there is frequently enough constriction to interfere with its normal conductivity, and, unless this is prevented, of course the operative procedure becomes useless. Likewise, a tenoplasty, although joining the tendon ends, will not permit its muscle to properly functionate unless we are able to prevent the formation of adhesions at the site of the operation. While the employment of the Cargyle and other membranes, to ensheath the nerves and tendons after they have been united, has done much to prevent the formation of adhesions, nerve union particularly has only met with a moderate degree of success. If massage were employed over a long period of time in all of these cases, we believe that the results would be more encouraging.

As soon as the wound is sufficiently healed and the soreness has disappeared, the operator should begin with gentle kneading of the tissues surrounding the incision. The flesh should be lifted up and carefully rolled beneath the fingers. When the incision has completely united and there is no tenderness, then the site of the operation is ready for manipulations. The skin and underlying tissue should be lifted up and gently stretched in the opposite direction from the course of the nerve or tendon. The degree of force employed should be slowly and carefully increased. In addition the entire limb must receive vigorous treatment and the neighboring joints be duly exercised with passive and active movements. One cannot expect to accomplish much unless the treatments are regularly and skilfully given over a long period of time.

REFERENCES

The list of references which follows includes, for the most part, only those publications of comparatively recent date. Its object is to give to the reader the names of authoritative works which he may consult in case he desires further details on any subject here treated. A very complete bibliography is to be found in Bum's "Handbuch der Massage und Heilgymnastik."

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CHAPTER VII

MECHANOTHERAPY

Charles Ricksher

Physicians have many methods for restoring diseased organs and for rendering them capable of functioning properly. Formerly drugs and rest were considered the only methods available; but, in the early part of the nineteenth century, Ling of Sweden formulated a series of exercises which would aid in restoring tone to the diseased parts by increasing the flow of blood through the muscles, and thus influence the general metabolism. One may be said to be healthy when his organs are functionating properly. One of the most important general functions of the body is that of nutrition, by virtue of which waste is repaired and the body maintains the integrity of its tissues and develops its different parts. The function of oxygenation and assimilation of food products is common to every living tissue, but in none of them does it reach such a high degree as in the muscles.

About half the body weight is made up of the muscles, and they play a very great part in body nutrition. When exercised regularly they become developed and strengthened, and, as they develop, so do the other parts of the body. With insufficient exercise or non-use of the muscles they deteriorate, and the general health and the general resistance of the whole body decreases. One who takes exercise regularly and faithfully remains in much better physical and mental condition than one who lives a sedentary life. But, in order to be of value, the exercise should be regular and should not lead to great fatigue. Even moderate exercise, which would in no way affect a normal man, will have a bad effect on one suffering from some heart lesion or from advanced arterial disease. Walking may be injurious to the latter, because, in walking, many muscles are used, not only those used in locomotion, but those used in maintaining equilibrium.

All gymnastic exercises demand the use, not of a single muscle or group of muscles, but call for the coöperation of a large number. In the ordinary gymnastic exercises we are unable to estimate exactly the amount of energy expended in the associated contractions of the cooperating muscles, even though we may measure fairly accurately the

amount necessary for the performance of any single motion. In ordering exercise for debilitated patients, and especially those suffering from cardiac disease, it is necessary to recognize and to take into consideration the gross effect of the movements on the various organs.

The general influence of exercise is, therefore, to develop the muscles and the other parts of the body. Continuous active voluntary movements soon cause fatigue, but this will soon disappear if one uses passive movements for a short time. This shows that the fatigue products caused by the muscular contractions have been removed by the blood, and that the passive movements do not cause as much tissue destruction as do the active ones. The increased muscular metabolism causes hunger and the production of heat, showing the direct effect of exercise upon the body economy.

The muscular action not only causes increased strength and resistance to external disorders in the parts used, but causes changes in the internal organs. Experience shows that exercise has a direct influence upon the flow of the blood, as evidenced in the increased pulse rate and flushed skin. Exercises increase blood pressure in the vessels in the muscles themselves, as well as in the larger vessels inside the chest wall. The pressure of the contracting muscle tissue affects the veins as well as the arteries, and causes a slowing in the rate of flow in the veins and an increased pressure in the latter. The artery walls are firm and the decrease in the size of the lumen of the vessel is less than in the veins. The valves of the heart prevent a regurgitation of the arterial blood, and it is hurried forward just as in the veins the valves prevent a reflux into the smaller vessels, and the blood is forced onward in the direction of the heart. Certain muscular movements cause a lengthening or shortening of the vessels, and the volume of blood is increased or diminished. In the neighborhood of the large joints the superficial vessels are bound down by the fascia, which tightens when the joints participate in some movements, and causes the vessels to empty; and, as the movements cease and the fascia relaxes, the blood is sucked into the empty vessels. In this way is explained not only the general influence of exercise upon the blood stream, but also the definite local action, increasing the flow in a part or slowing the current in another.

But besides this there is a very important influence upon blood formation and the preservation of the normal chemical constitution. In order that the blood be able to functionate with the greatest degree of efficiency, it must flow to the various parts of the body, obtain the substances necessary for its own composition and for the nourishment of the whole body; and, to discharge its full duty, it must remove broken-down material from the various parts and carry them to the proper excretory organs, the skin, kidneys, lungs, etc. In this way the blood maintains a certain average between the intake and output of the body.

Since, as we have shown, bodily movements have not only a general influence on the blood stream, but also a local action in various parts of the body, one would be warranted in drawing the conclusion that under certain conditions they would have a beneficial effect in disturbances of health, especially in cases where the blood flow is disordered by some valvular or muscular defect.

By means of systematic, well-ordered exercise, the size of the chest cavity is increased, more air is taken in, and the blood is more quickly oxygenated. The arterial trunks and the larger veins all tend to be continuously dilated by the elastic pull of the lungs, a pull which increases at each inspiration. The elasticity of the lungs and the contractions of the muscles of inspiration thus lighten the work of the right ventricle as well as that of the left.

The appetite is increased, and this usually means a general upbuilding of the whole body. While the majority of the muscles of deglutition and digestion are of the involuntary type, they are influenced to a great degree by the voluntary muscles, and, as the latter are strengthened, so is the involuntary musculature of the intestinal tract.

The excretion of decomposition products is favored in every way. As the capacity of the lungs is increased, a larger amount of air is expelled and the blood is relieved of a larger amount of carbon-dioxid. The peristaltic movements in the intestine are quickened, and indigestible fecal masses are expelled. In this way constipation and its attendant inconveniences are avoided. Sweat secretion is stimulated, and much effete matter is thus discharged.

Perhaps the most beneficial general effects of exercise are seen in the workings of the central nervous system. The irritability and tendency to emotional outbursts, the easy excitability and general timidity frequently seen in those who live a confined or sedentary life, are all absent in those who devote much time to active outdoor life, or who indulge in regular gymnastic work. In the latter the muscles respond more readily to stimuli, the movements are more prompt, and the desired action is performed more easily and with less expenditure of energy.

The great disadvantage, however, of exercise, in which the patient is given certain movements which he is supposed to perform, or which some one aids him in performing, is that the energy expended cannot be calculated. The patient is too active, and calls forth an excess of energy, or the assistant does not gauge his aid correctly. This led Zander to devise several pieces of apparatus by which the force and amplitude of each movement are determined precisely. By means of a movable weight the dosage is always determined beforehand, and it does not vary from day to day (as it would in a purely manual method), provided the balance weight occupies the same position on the lever. There have been several kinds of mechanical apparatus put forward, each of which has

many supporters. In America Dr. Sargent of Harvard has a system devised for the cultivation of special groups of muscles. This system is not nearly so complete as some of those used in Europe, but is of value in certain cases. The machines devised by Emil Zander of Stockholm form the most complete system of mechano-therapy at present. Herz and Krukenberg have contrived systems which in many ways are similar to Zander's. The aim of all of these systems is to avoid the use of an attendant, who, in the ordinary Swedish gymnastic exercises, must be a skilled operator.

By means of the machines active, passive, and resisted movements, vibration, and percussion may be performed at a much less cost to the patient, and, if a well-equipped "Institute" is at hand, with much more accuracy than by manual methods. Since the Zander system is the most fully developed and the one most frequently used in this country, we will confine our attention to it. The two classes of these machines are designed for the production of active, active-passive, and passive movements; and for vibration and massage. The latter two groups will be considered under the heading of mechanical percussion.

ACTIVE APPARATUS

The mechanical device by which a properly graduated resistance is obtained in the so-called active machines, i. e., those which are set in motion by the muscular effort of the patient, in contradistinction to the passive machines which are operated by a motor, is the raising of a weighted lever through an arc of 180°. When this lever hangs perpendicularly downward it requires but slight force to move it out of the perpendicular; as it advances toward the horizontal position the effort required to move it onward rises to a maximum; as it proceeds toward a position perpendicularly upward, it again requires a diminishing amount of force to continue its onward movement.

This sinusoidal curve of resistance corresponds very closely with the curve of the disposable force of a contracting muscle. Thus, in the apparatus A 6, for abduction of the arms, the resistance is the greatest when the arm is abducted at an angle of 75 degrees to 80 degrees, a point where the greatest muscle strength is developed. And in every machine the sinusoidal curve is so arranged that the greatest resistance comes at the point where the greatest muscle power is developed.

The advantages claimed for these machines as stated by van Dortmond are: (a) The direction of each movement is a fixed and determined one, and demands for its execution the action of a single muscle group; (b) the amplitude of each movement is regulated with the greatest exactness; (c) the construction of the apparatus is such that, during each

moment of the movement performed, the resistance of the apparatus corresponds exactly to the amount of force disposable by the muscle, so that the muscular exertion is always equal, all through the course of the movement.

The following list of active apparatus with the muscles used and respiratory rhythm is quoted from Hasebroeck (18):

Series A.—Active Movements of the Arms

A 1. *Lowering of the Arms (Sideways)*

Muscles used: Pectoralis major and minor, latissimus dorsi, teres major, posterior third of the deltoid, anconeus longus, rhomboideus, levator anguli scapulæ; also the flexor muscles of the trunk on the side of the movement, in order to avoid bending the trunk to the opposite side.

Respiration: After deep inspiration, expiration during sinking, inspiration during raising.

A 2. *Raising of the Arms; Raising of the Shoulders*

1. **Raising of the Arms.**—*Position a:* Arms hanging at the side. Movement of the outstretched arms forward and upward, upward and backward, lowering them.

Position b: Forearm flexed on the arm. Movement striking upward, downward.

Muscles used: Shoulder, girdle, and arm muscles; deltoid, supraspinatus, caput longum bicipitus; serratus anticus, trapezius, triceps; also in raising the outstretched arm forward, the long back muscles of fixation and the maintenance of equilibrium.

Respiration: Inspiration during raising, expiration during the downward movements.

2. **Raising of the Shoulders.**—*Position:* Arm hanging by the side. Movement of the shoulder girdle above forward, upward and backward, downward to the position at beginning.

Muscles: Upper half of the trapezius, pectoralis major, latissimus dorsi.

Respiration: Inspiration during the whole movement, expiration in the pause.

A 3. *Bending of the Arms and Lowering the Same*

Muscles: Pectoralis major, latissimus dorsi, teres major, posterior third of the deltoid, anconeus longus, rhomboidei, levator anguli scapulæ, pectoralis minor, biceps brachii, brachialis internus.

Respiration: After deep inspiration, expiration during the drawing in of the hand-grips, expiration during the upward movement of the arm.

FIG. 1.—ZANDER APPARATUS FOR BENDING AND LOWERING THE ARMS.

Action on the thorax: Widening.
N. B.—Chest out, elbows back.

A 4. *Stretching of the Arms Upward*

Muscles: Deltoid, supraspinatus, trapezius (claviculo-acromial portion), serratus anticus major, triceps brachii.

Respiration: Inspiration during the upward, expiration during the downward, movement.

N. B.—Body slightly bent forward, chest out.

A 5. *Adduction of the Arms*

Muscles: Pectoralis major.

Respiration: Inspiration during the adduction, expiration while the arms are returning to their original position.

Action on the Thorax: Widening as well during the abduction as during the adduction.

Fig. 2.—Zander Apparatus for Adduction and Abduction of the Arms.

A 6. *Abduction of the Arms*

Muscles: Latissimus dorsi, posterior third of the deltoid, trapezius, rhomboideus, pectoralis minor, serratus anticus major.

Respiration: Inspiration during abduction, expiration during adduction.

Action on the Thorax: Resistance diminished against the inspiratory muscles.

A 7, a. *Circling of the Arms*

Muscles: Pectoralis major, latissimus dorsi, teres major, rhomboidei or deltoid; supraspinatus, serratus anticus major.

Respiration: Inspiration during the first and second, expiration during the third and fourth revolution.

A 7, b. *Circling of the Hands*

Muscles: A more or less general use of the forearm muscles in a changing succession through the impulse to a change to an active-passive movement.

A 8, a. *Rotation of the Arms, Pronation and Supination*

Muscles: Either the pronators of the hand and adductors of the arm or the supinators and abductors. Pronator teres and quadratus radialis internus, brachio-radialis, subscapularis, teres minor; latissimus dorsi; or the supinator brevis, radialis externus longus and brevis, brachio-radialis, biceps brachii, infraspinatus, teres minor.

A 8 b. *Rotation of the Arms (Active-passive)*

Muscles: The same as in A 8, a.

A 9. *Flexion of the Forearms*

Muscles: Those on the flexor surface of the arms. Biceps, brachialis internus, brachio-radialis, pronator teres, flexor digitorum, communis, profunda, and sublimis.

Respiration: Inspiration during flexion, expiration during extension.

A 10. *Extension of the Forearms*

Muscles: Those on the extensor surface of the arms, and the back muscles which hold the arm against the apparatus. Triceps brachii and anconeus quartus, latissimus dorsi.

Respiration: Inspiration during extension, expiration during flexion.

N. B.—A 9 and A 10 may be combined, and by the insertion of a weighted pendulum may be changed to an active-passive apparatus.

A 11. *Extension and Flexion of the Hands*

Muscles: The flexors and extensors of the hands. Radialis internus, palmaris longus, ulnaris internus, flexor digitorum communis, or the radialis externus longus and brevis ulnaris externus.

Respiration: Inspiration during the active movement, expiration during the passive return of the hand.

A 12. *Extension and Flexion of the Fingers*

Muscles: Interossei and lumbricales (I phalanx), flexor sublimis digitorum (II phalanx), flexor profundus digitorum (III phalanx), or the extensor communis digitorum, extensor indicis proprius. Extensor digiti quinti proprius (I phalanx), interossei and lumbricales (II and III phalanges). In isolated movements of the thumb the abductor pollicis longus et brevis, extensor pollicis longus et brevis (extension and abduction) are used. The flexor pollicis longus et brevis, adductor pollicis, opponeus pollicis are used in flexion, adduction, and opposition.

Series B.—Active Movements of the Legs

B 1. *Flexion of the Hip*

Muscles: Ilio-psoas, tensor fasciæ latæ, rectus femoris, sartorius.

Respiration: Inspiration during flexion, expiration during the sinking of the leg.

B 2. *Extension of the Hip*

Muscles: Gluteus maximus, medius, and minimus; biceps femoris, semimembranosus, semitendinosus, gastrocnemius.

Respiration: Inspiration during the extension, expiration during flexion.

B 3. *Hip-knee Flexion—Raising of the Hip*

Muscles: For hip-knee flexion—ilio-psoas, tensor fasciæ latæ, sartorius, biceps femoris, semimembranosus, semitendinosus, gracilis, tibialis anticus, extensor digitorum et hallucis longus, peroneus tertius, gluteæ. For raising the hip—Gluteus medius et minimus, sacrolumbalis, obliqui abdominis externus et internus.

Respiration: Inspiration during extension of the leg; expiration during flexion.

B 4. (*a*) *Hip-knee Extension;* (*b*) *Lowering of the Hip*

Muscles: For (a), gluteus maximus, medius, and the posterior one-third of the minimus, quadriceps femoris, triceps suræ, peroneus longus

FIG. 3.—ZANDER APPARATUS FOR HIP-KNEE EXTENSION AND FOR LOWERING THE HIP.

et brevis, tibialis posticus. For (b), iliopsoas, pectineus, adductors, sacro-lumbalis, obliquus abdominis externus and internus.

Respiration: Inspiration during extension, expiration during return.

B 5, a. *Adduction of the Legs, Sitting*

Muscles: Adductors, gracilis, pectineus.

Respiration: Inspiration during adduction, expiration during abduction.

B 5, b. *Adduction of the Legs, Half Reclining with Bent Knees*

Muscles: As in B 5, a.
Respiration: As in B 5, a.

B 6. *Abduction of the Legs*

Muscles: Gluteus medius and minimus, pyriformis, obturator internus, gemelli.
Respiration: Inspiration during abduction, expiration during adduction.

B 7. *Cycling*

Muscles: Gluteus maximus, quadriceps femoris, triceps suræ.
Respiration: About two revolutions to each inspiration and expiration.

B 8. *Rotation of the Legs*

Muscles: Quadriceps femoris, obturator, externus and internus, pyriformis, gemelli, posterior part of the gluteus medius, extensor digitorum longus, peroneus tertius, longus and brevis, abductor digiti quinti, gluteus medius, and anterior two-thirds of the gluteus minimus, tensor fasciæ latæ, tibialis anticus and posticus, abductor hallucis.
Respiration: Inspiration during the resistance movement, expiration during the withdrawal of the foot.

B 9, *Flexion of the Knees*

Muscles: Biceps, semimembranosus, semitendinosus, gracilis, sartorius, gastrocnemius.
Respiration: Inspiration during flexion, expiration during the extension.

B 10. *Extension of the Knees*

Muscles: Quadriceps femoris, and tensor fasciæ latæ.
Respiration: Inspiration during extension, expiration during flexion. In the second half of the movement the abdominal muscles may be strained if care is not taken, especially in the case of women and weak persons.

By the insertion of a pendulum the movement of the combined B 9 and B 10 apparatus may be made an active-passive one.

B 11. *Extension and Flexion of the Feet*

Muscles: Gastrocnemius, volcus, tibialis posticus, peroneus longus or tibialis anticus, extensor digitorum et hallucis longus peroneus.

FIG. 4.—ZANDER APPARATUS FOR CIRCUMDUCTION OF THE FOOT.

B 12. *Circumduction of the Feet*

Muscles: The same as in B 11. The thigh should be fixed.

B 13. *Spiral Turning of the Feet—Pronation and Supination of the Feet*

Muscles: (a) Pronation—triceps suræ, tibialis posticus, flexor digitorum, and hallucis longus. (b) Supination—peroneus tertius, extensor digitorum longus, and the mesial half of the musculature of the sole of the feet.

Series C.—Active Movements of the Trunk

C 1. *Bending of the Trunk Forward, Sitting*

Muscles: Iliopsoas, tensor fasciæ latæ, rectus femoris, rectus abdominis, obliquus externus and internus.

Respiration: After a deep inspiration in the starting position, expiration during the bending forward, then inspiration and expiration during recovery (during the latter part of the movement back the tension of the abdominal muscles favors expiration).

C 2. *Expansion of the Trunk, Sitting*

Muscles: Erector spinæ, trapezius, rhomboidei, levator anguli scapulæ, latissimus dorsi, gluteus maximus, biceps femoris, semimembranosus, semitendinosus. As fixators of the knee joint, vastus lateralis and medialis; of the ankle joint, triceps suræ, tibialis posticus, peroneus longus and brevis.

Respiration: Inspiration during the erection and inclination backward until the back touches the bench, expiration during the return movement to the first position.

C 3. *Bending and Raising the Trunk, Lying*

Muscles: Iliopsoas, tensor fasciæ latæ, rectus femoris, rectus abdominis, obliquus externus and internus, transversus.

Respiration: Deep inspiration in the lying position, expiration during the inclination forward and bending over; inspiration while bending backward; expiration while sinking back to the lying position.

C 4. *Extension of the Trunk, Sitting with Stretched Legs*

Muscles: The same as in C 2. However, in the earliest stage of the movement one finds a strong contraction of the gluteus maximus and the posterior thigh muscles. Furthermore, contrary to C 2, in the backward sinking of the trunk the counterpoise gradually overcomes the resistance so that the abdominal muscles are stimulated to a strong negative contraction.

Respiration: Inspiration during the inclination and sinking backward; expiration while inclining forward.

N. B.—Stop the sinking backward when the contraction of the abdominal muscles becomes noticeable.

C 5. *Extension of the Trunk, Standing*

Muscles: The same as in C 2, yet in the standing position the extensors of the back, the erectores spinæ, will be more influenced.

Respiration: Inspiration during the backward movement, expiration during the forward movement.

N. B.—The thighs should not be removed from the cross piece.

C 6. *Bending the Trunk Sideways*

Muscles: Quadratus lumborum, serratus posticus inferior and intertransversarii as true flexors to the side. Iliocostals, levatores costarum, and obliquus externus and internus as muscles which also have a backward drawing component. Latissimus dorsi, teres major and minor, pectoralis major and minor, rhomboidei, lower half of the trapezius, serratus anticus major, levator anguli scapulæ.

Respiration: Inspiration while bending sideways; expiration while returning to the first position.

Action on the Thorax: Widening of the side which is not active.

C 7. *Rotation of the Trunk*

Muscles: Obliquus abdominis internus, transversus, serratus posticus inferior, semispinalis dorsi, multifidus spinæ, rotatores dorsi, obliquus externus, serratus anticus major, trapezius, rhomboideus.

Respiration: Deep inspiration in the first position; expiration during the resisted turning; inspiration during the return to the first position and in the pause.

C 8. *Rotation of the Pelvis*

Muscles: The same as in C 7.

Respiration: Inspiration in the first position, expiration during the resisted turning, inspiration during the return to the first position and in the pause.

C 10. *Bending of the Neck*

Muscles: In extension, the trapezius, splenii capitis et cervicis, iliocostales cervicis, longissimi capitis and cervicis, semispinalis cervicis and capitis, spinales cervicis, rectus capitis posticus major and minor. In bending sideways the same muscles, and in addition the intertransversarii and rectus capitis lateralis. In turning diagonally the sternocleidomastoidei, scaleni, longi colli, atlantis and capitis, rectus capitis anterior.

PASSIVE MOVEMENTS

Passive movements is the term used to designate the movement of one or more joints in a methodical manner by means of some external force. This force may be the hands of the operator or some mechanical apparatus. They are used to break up adhesions in joints, pseudoankyloses, dissolve exudates, to correct atrophies due to disuse, and for motor disorders due to nervous diseases.

In cases where severe muscular exercise is contraindicated, as in individuals suffering from some forms of heart disease, or in certain nervous diseases where it is impossible for the individual to perform active movements, as in hemiplegics and those suffering from a general neuritis, this form of exercise is of the greatest value. The muscles receive the greatest amount of exercise with the least exertion to the patient. In the cases where mechanical apparatus is used, the apparatus can be accurately gauged to the patient's condition, and great fatigue is avoided. While each movement is limited by the apparatus, the attention of the operator can be directed to the respiration, time of movement, and the condition of the patient. In movements of the trunk especially, it is important that the rhythm of movement and that of the respiration should be fixed and definite. The respirations should be deep and correspond to the changes in the volume of the chest produced by the movement. In movements of the extremities it is not so necessary to watch the respiration.

In the Zander system the apparatus is designed to be driven by electrical, gas, or steam power. The passive apparatus are as follows (18):

Series D.—Balancing Movements

This series comprises the apparatus which are also called active-passive, because, while the movement is caused by the moving apparatus, there is also a negative contraction of the muscles involved.

D 1. *Balancing of the Trunk (a) Forward, (b) Sideways*

Muscles: For (a)—The flexor and extensor muscles of the trunk and thigh, as in C 1 and C 2. For (b)—The muscles which bend the trunk sideways, as in C 6. Also the flexor muscles of the legs for fixation of the thigh on the pelvis.

Respiration: The highest possible adjustment to the rhythm of the movement so that there are two swinging movements to each inspiration and expiration. The movement lasts 1 to 3 minutes.

D 2. *Circling of the Trunk, Sitting with Legs Closed*

Muscles: The muscles causing forward, backward, and side flexion (see C 1, C 2, C 6, B 1, B 2).

Respiration: As in D 1. The movement lasts 1 minute to each direction.

FIG. 5.—ZANDER APPARATUS FOR CIRCLING OF THE TRUNK, SITTING SADDLEWAYS.

D 3. *Circling of the Trunk, Sitting Saddleways*

Muscles: As in D 2, the position on the saddle also calls the muscles of the thighs into play.

Respiration: As in D 1 and D 2. The movement lasts one minute to each direction.

The active apparatus A 7, a, A 7, b, A 8, b, A 9 and A 10, B 7, B 9 and B 10, B 11, B 12, B 13, may also be used as active-passive apparatus.

The following apparatus is used exclusively for passive movements:

Series E

E 2. *Extension and Flexion of the Hands (Passively)*
E 3. *Adduction and Abduction of the Hands (Passively)*
E 4. *Extension and Flexion of the Fingers (Passively)*
E 5. *Circling of the Legs in the Hip-joint*

Action: Stretching of the joint capsule of the hip, knee, and ankle joints. Perhaps also some stretching of the sciatic nerve.

E 6. *Dilatation of the Chest, Artificial Breathing*

Action: Alternating stretching of the muscles and fascia of the vertebra and the walls of the thorax, so as to cause a dilatation. Stimulation to deep inspiration and filling of the apex of the lungs through passive widening of the thorax, especially the upper part. Mobilization of a stiffened thorax.

Respiration: Inspiration with the extension up to the point where the abdominal muscles become tense, then expiration during the return to the first position. The expiration if possible should be prolonged until the beginning of the next movement.

E 7. *Rotation of the Trunk (Passively)*

Action: Alternating stretching of the numerous ligaments and extensor muscles of the trunk. Mobilization of the vertebra and the lower thorax. Compression and expansion of the viscera, especially during inspiration.

E 8. *Raising of the Pelvis (a) Forward, (b) Sideways, (c) Lying Backward*

Action: For (a)—Lowering the pressure in abdominal cavity. Increased blood flow to the diaphragm and into the thorax from the organs in the true pelvis, which is accomplished by the increased level from the pressure from above and in front. Stretching of the ligaments holding the organs in the true pelvis.

For (b)—Extension of the trunk and the stretching of those muscles which participate in a side movement of the thorax above the pelvis.

For (c)—Only in men, passive pressure and extension of the trunk from behind forward. Passive tension of the abdominal walls.

THERAPEUTIC USES OF THE VARIOUS APPARATUS

While the various movements and exercises are designed primarily for those suffering from disease, they are of value to many people who have neither time nor inclination to take active outdoor exercise. For many men of sedentary habits a course in the various exercises causes a general toning up of the muscular and nervous systems and allows them to do better work.

In those suffering from general debility or convalescent from some acute illness, mechanotherapy is a means of the greatest value in achieving a definite cure. If at the beginning the patient is not strong enough to perform the more active exercises, passive movements, massage, and vibratory movements will aid in toning up the general muscular and nervous systems. Later the active-passive and active movements may be used with benefit. The exercises should be of short duration, and, in the old and very debilitated, should at first be used only two or three times weekly. It is of the greatest importance to avoid fatigue, and by a gradual progression and careful dosage one may achieve this.

In chlorosis and anemia the exercises increase the capacity of the chest with consequent increased oxygenation of the blood and improvement of the general nutrition. The active-passive movements are used carefully, later followed by the active. In many cases of nose bleeding the apparatus C 1, C 2, A 3, A 4 should be avoided, and only those prescribed which will tend to increase the circulation in the limbs and trunk.

In gout there is some anomaly in the metabolic processes by which the products of incomplete oxidation accumulate in the blood. In these cases the increased oxidation caused by muscular work must do good. In the acute exacerbations rest is indicated, but in the intervals, and for the removal of the gouty disposition, mechanotherapy practiced carefully and systematically will cause many gouty subjects to remain a longer time from attacks. Massage and passive movements prevent the stiffening of the joints and tendons and the laying down of the chalky deposits. For the joints attacked by the disease rhythmical active-passive and passive movements are required. Manual massage is of value in the swollen joints used conjointly with the movements.

In diabetes the therapeutic value of muscular exercise is recognized by all authorities. In the lighter forms systematic, well-supervised muscular exercise causes the sugar to disappear; and in the less severe cases there is a decrease in the amount excreted in the urine. The functional nervous troubles accompanying this disease are usually supposed to be due to some autointoxication and disappear on the removal of the cause.

In all forms of obesity any system of exercise is of great advantage. All the muscles of the body should take part in the movements, and con-

sequently the more generally recommended methods, such as walking and mountain climbing, are not of the highest value. The frequent complication of fatty myocarditis requires careful observation, and for this reason indiscriminate exercise may be harmful. The movements of the trunk reduce the fatty abdomen, increase intestinal peristalsis, increase the visceral circulation, and tend to reduce the intra-abdominal pressure and to relieve the impairment of function of the diaphragm. In treating the localized deposits of fat, the percussion apparatus in conjunction with exercise is required.

In disease of the respiratory system exercise is of value in preventing, as well as in curing, disease. Physicians generally now recognize the importance of keeping the resistance of the lungs as high as possible, and this can only be accomplished by widening the thorax so that the intake of air is increased. The active movements comprise the exercises designed to exercise and strengthen the muscles of respiration. The simplest exercise is to methodically take the deepest possible inspirations and expirations while sitting or standing in the open air, repeated many times in a rhythmical manner.

For strengthening the inspiratory muscles one employs the apparatus for raising and lowering the arms, A 1 and A 2; stretching the arms upward, A 3; for adduction and abduction of the arms, A 5 and A 6; abduction of the legs, B 6· extension of the hip, B 2; and bending the body forward, C 1.

For strengthening the expiratory muscles, one uses the apparatus for flexion and extension of the forearms, A 9 and A 10; flexion of the knees, B 9; adduction of the legs, B 5, a; bending the trunk forward and sideways, C 1 and C 6; and rotation of the pelvis, C 8. In all cases the weights should be carefully adjusted to the individual's capacity, as in every other exercise.

The passive widening of the thorax is performed either with the help of the shoulder girdle or through movements of the vertebra. The Zander apparatus, E 6, is of the greatest value in this exercise. Passive movements of the trunk act by rhythmical compression and expansion of the ribs, the chest and abdominal cavities are widened and narrowed.

Prophylactically the movements are used in young individuals with weak, flat, poorly developed chests, or in persons who are inclined to frequent attacks of catarrh or diseases of the respiratory organs, therapeutically in diseases of the lungs themselves. By means of this treatment we get general effects fitted to obviate the results of respiratory insufficiency, and to improve the general nutrition through the more complete oxygenation of the blood and local effects on the circulation, and on the nutrition of the lung tissue.

In chronic bronchitis there is usually a tendency to superficial respiration and insufficient circulation. In patients suffering from this disease

daily exercise with respiratory exercises will improve their condition in a few months. After pleurisy and pneumonia, the convalescence is shortened and the tendency toward adhesions is diminished by the use of exercise. In chronic pleurisy the prompt return to deep and energetic respiratory movements is the only effective means of battling against the formation of adhesions. In well-marked cases of pulmonary tuberculosis active respiratory movements are contraindicated, and they can be used only in the early stages. In emphysema the condition is frequently improved by betterment of the circulation. In bronchial asthma good results are obtained not only by the improvement of the respiration, which frequently is superficial and irregular, but also by the psychic effect of the apparatus.

For the last hundred years the good results following systematic exercises have been recognized in the treatment of heart cases. Ling was the first to devise a systematic series of exercises for these cases. In Germany a combination of baths and exercise known as the Schott treatment has been used for the last twenty-five years. Recently, through the work of Nebel, the mechanotherapeutic apparatus has been brought to the front, and good results have been reported. Wide early spoke of the lessening of the work of the heart by improvement of the weakened circulation. In speaking of this, Hasebroeck says that it is important to recognize that the necessary increase in rapidity of the blood flow can be obtained by increasing the work of propulsion on the side of the central system as well as aspiration on the side of the peripheral system.

Zander's aim was in many ways similar to Oertel's, "emptying of the venous system by improvement of the general circulation, bettering the condition of the heart muscle, which is stimulated to increased activity by a slowly increasing demand, and restoration or reconstruction of a compensatory hypertrophy." Zander sought to empty the venous system by a better general circulatory condition, just as did Ling. The Schott system aims at increasing the tonicity of the heart muscle, and tachycardia and dyspnea are carefully avoided.

The action of muscular work must be sharply differentiated from the action of gymnastic movements. The increased rate of the blood stream in the movements is limited to the part of the body taking part in the movement, with the exception of movements of the trunk, which tend to increase the amount of blood in the right ventricle. The sudden overfilling of the right heart is not desirable, since the pulmonary circulation is usually engorged, and bad results may follow such a contingency. The active-passive movements are especially useful in cardiac cases, since they can be continued for a long time without fatiguing the patient, and tend to calm the nervous and circulatory systems. The active movements tend to increase the pressure in the peripheral circulation and increase the pulse rate.

In all acute stages of endocarditis and pericarditis, in acute and chronic inflammations of the heart muscle, in aneurysms and thrombi, rest is required and all exercises are contraindicated.

In valvular defects, before compensation is established, rest is indicated; when compensation is established it is desirable to strengthen the heart muscle and to maintain equilibrium; while, in conditions of broken compensation, one must observe the action of the heart muscle as well as the valvular defects.

The most frequent valvular defect is a mitral insufficiency. In the majority of cases compensation is easily established and maintained and occasionally the symptoms may entirely disappear. In this disease the rapidity of the contraction of the heart muscle is very important, and the aim of therapy is to strengthen and to slow the contractions. This is done by the use of mild active movements followed by passive movements, gradually increasing the dose of active movements so that the strength of the heart muscle is increased.

In mitral stenosis the left ventricle is filled more slowly than normally, and everything which tends to reduce the pulse rate should be avoided. In such a case one uses the movements which lead to an improvement in the peripheral circulation, such as the pronation and supination of the arm, A 8, a; circling of the hand, A 7, b; circling of feet, B 12; pronation and supination of the feet, B 13. In order to strengthen the weakened left ventricle, one must gradually use active movements and carefully watch the pulse rate.

In aortic insufficiency the heart hypertrophies to a great degree and its work is heavy. In such cases care should be taken to decrease the peripheral resistance as much as possible, and only exercises which tend to calm the heart should be used, such as A 11, hand flexion and extension; A 9, forearm flexion; B 9, flexion of the knees, and B 10, extension of the knees.

In fatty myocarditis movements which increase the work of the heart should be avoided, and all exercises should be carefully supervised. Such movements as B 7, cycling, are of value.

Arteriosclerosis is frequently a factor in fatty myocarditis, and leads to an increased blood pressure. In such cases the kidneys especially are affected, and this leads to a general letting down of the resistance of the entire body. The general circulation is always more or less affected; and the muscles, which normally contain a very large amount of the blood, cannot get rid of their waste products. By means of mechanotherapy the peripheral circulation is stimulated and a general improvement in the general condition results. When there is an arrhythmic or intermittent pulse, showing the presence of some degeneration of the heart muscle, especial care must be taken not to increase the work of the heart. When, however, the heart muscle is not seriously degenerated, although there

may be some cardiac hypertrophy, active movements are of value, especially those which cause a more active intestinal peristalsis. Vibration to the chest and abdomen is frequently indicated to cause a more regular heart beat and to stimulate the abdominal viscera.

Cardiac neuroses are generally a part of more general neurotic conditions and are much benefited by this system. Active exercises with considerable resistance, which may cause some palpitation at first, cause the heart to become more quiet and the rhythm more regular. The cardiac neurosis may be the beginning of an arteriosclerotic condition, or may be due to some gastric or intestinal disturbance. In such cases the treatment should be primarily for these conditions.

Chronic constipation, gastric dilatation, and the so-called hepatic congestion are disorders common to a large sedentary class. They are in part due to the lack of general exercise, and especially to a lack of movements which bring the abdominal muscles into play. Mere walking does not cause them to bend the trunk forward, to stoop, to raise themselves again to an erect posture—movements which would cause these muscles to contract. These conditions are rarely found in the laboring classes who perform hard work, but are especially common among those with occupations which require little exercise. In women who destroy the abdominal muscles by the use of corsets they are very frequently found.

In chronic constipation use is made of those methods which tend to provoke the spontaneous play of the intrinsic and extrinsic forces of peristalsis. Massage produces a rapid improvement of the condition, but a more lasting effect is produced by the exercises which tone up the abdominal muscles. In very severe cases, after a few weeks' treatment without appreciable results, one should supplement the exercises with diet, hydrotherapy, and electricity. Hasebroeck recommends the following apparatus: F 1, vibration of the different parts of the body; B 8, rotation of the legs; C 8, rotation of the pelvis; D 1, balancing of the trunk; E 6, dilatation of the chest; E 5, circling of the legs in the hip joint; H 1, kneading of the abdomen; J 6, circular friction of the abdomen; G 3, percussion of the legs.

In the functional nervous disorders the maintenance of nutrition and the improvement of the circulation are of great value. The Weir Mitchell rest cure includes massage and a certain number of passive exercises which are necessary for the improvement of the nutrition of the muscles. The psychic effect of a large mass of apparatus is not to be ignored in these conditions. Very frequently the patients require some tangible evidence that they are being treated, and this is supplied by any of the pieces of apparatus. In weak patients passive movements only should be used at first, but the active movements should be added as soon as possible. In the patients who are not debilitated the active exercises may be begun at once. The movements involving the upper extremity with slight

resistance train the patient to pay attention to the rhythm and increase his will power. At the same time his attention is taken off his own illness. In hysteria with respiratory seizures, movements involving the respiratory organs and requiring a regular respiration are of value, not only in the mental training received, but also in the formation of habits of correct breathing.

In disorders of the sensory nerves vibration and massage are of the most value, and these disorders will be treated under that heading. However, the general physical condition is also to be observed and the general nutrition improved by the use of the more generalized movements.

Motor disorders are treated by active as well as by passive movements. Contractures are especially frequent in the various forms of peripheral neuritis, traumatic myelitis, and certain forms of apoplexy, and may be actively combated by means of the active-passive and passive movements. In conditions in which there is extensor weakness of the foot the apparatus B 12, for circumduction of the feet, is especially useful. By its use the normal movements of the foot are more quickly regained than by any other exercise. In spastic conditions some benefit may be gained by strengthening the antagonists of the muscles involved, but the improvement is usually of short duration. In tabes the hypotonia is often marked, and this, as well as the general circulatory condition, may be improved by means of mechanical exercise. The general vibratory movements, in conjunction with Frenkel's exercises, are of special value in this disease.

MECHANICAL PERCUSSION

By this term is meant the more or less rapid tapping of the body by means of a specially constructed instrument. The rapidity and force of the blows can be more accurately determined in this way, and they can be kept up for a longer time than in manual percussion.

The action of the percussion is essentially that of exciting muscular contractions, and especially affects the fibrillæ. Not only the superficial muscles are affected, but also even the underlying involuntary muscles. Kumpf has studied the action of percussion on the uterus and has found that it becomes harder, nears a spherical form, and decreases in length.

Mechanical stimuli act on nerves, if they can change the form of the nerve with a certain rapidity. Sensory nerves react with a painful sensation, motor nerves with a contraction of the part affected. On the blood vessels weak stimuli cause constriction, strong ones a dilatation following a transitory constriction. The hyperemia, so caused, is of especial benefit in causing the absorption of pathological transudates and exudates. The secretory and excretory glands are stimulated by percus-

sion of from five to ten minutes, the secretions being especially rich in water and lacking many or containing a less amount of the specific substances.

Lange has determined that slow percussions, up to a few hundred a minute, cause predominating mechanical action, very rapid strokes, of several thousand per minute, show an action corresponding to the use of a strong faradic current. Medium frequency causes an action between the two extremes. Long continuance of a medium frequency causes the same effect as a high frequency.

Vibratory massage in general has the same effect as manual, but it has the advantage of allowing itself to be more circumscribed and its action is usually more intense. The indications for it are the same as in manual massage, i. e., to increase muscle strength, to stimulate metabolism, to cause the resolution of transudates and exudates, to break up adhesions, and to stimulate the circulation to a part.

According to Bum, its use is contraindicated in every disease process in which products harmful to the organism are set free in the blood stream, as in acute inflammations, aneurysms, venous thrombi, malignant new growths, tuberculosis, syphilitic processes, gonorrhea, acute rheumatism, intoxications, etc. Its use is also contraindicated in ulcerated conditions of internal organs, as the stomach. Persons in advanced stages of arteriosclerosis should not be treated by this means. And in no case should a physician use this form of massage until he is sure of his diagnosis. The opportunity to do harm here is, as in every other mechanical procedure, too great to allow one to take chances.

Apparatus

The earlier forms of percussion apparatus were run by hand or foot power, but they were not satisfactory, as not enough speed could be reached, and the power could not be so long kept up as is desired. Compressed air and carbonic acid gas have also been used as motive power, and some of the manufacturers have been very successful.

In this country, however, the electrically operated apparatus is probably the best and most convenient. There are many forms on the market at various prices; but the cheap ones are apt to be unsatisfactory. Many of the portable vibrators are very undesirable; they wear out quickly and transmit so much vibration to the hand of the operator that they cannot be used for the length of time necessary. Various sized knobs, discs, rollers, and balls are used to transmit the vibration to the various parts of the body.

The apparatus is best used on the bare skin, the patient sitting or lying, so that every part is easily accessible. The apparatus should at

first be used with light pressure, which may be gradually increased. If the part is painful, the surrounding area should be treated, and the painful spot gradually approached. The patient's face should be watched in order to observe whether or not there is much pain.

Zander has also invented apparatus for percussion and general vibration, kneading of the abdomen, and friction. In all of this apparatus,

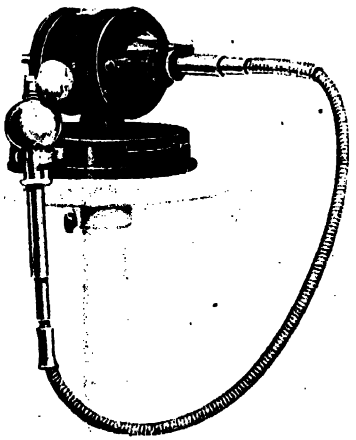

Fig. 6.—One Form of Mechanical Vibrator with Stand.
Electricity is used for motive force.

while the general effect is that produced by the smaller vibrator, there are also more general effects. The effect of horse-back riding—the general vibration of the whole body—can be obtained by his apparatus designated as F 2—while a more local vibration has only a superficial effect. The entire mucous membrane of the various parts of the body is stimulated, gastric and intestinal peristalsis is increased, and the voluntary musculature is toned up. Hasebroeck has found that in the circulatory system vibration causes:

I.—A decrease in the pulse frequency.
II.—Vasomotor heightening of the arterial tension.
III.—Increase in tonicity of the heart musculature.
IV.—Increase in the blood pressure.

As a therapeutic appliance the mechanical vibration has been used for disorders of every part of the body, and often with much success. In some diseases of the nose, ears, and eyes the chronic conditions are relieved to a great extent by treatments over a period of several weeks.

Ozena, chronic catarrh of the eustachian tube, chronic middle-ear disease, chronic forms of iritis, iridochorioiditis, and chorioretinitis are among the disorders which are greatly relieved by mechanical massage.

Excellent results are reported in disorders of the heart and circulatory apparatus. While the exercises of Ling and the mechanotherapy

FIG. 7.—ZANDER APPARATUS FOR MECHANICAL PERCUSSION.

of Zander have more influence on these conditions, localized percussion is often of some value—by decreasing the circulatory disorder and lessening, in that way, the work of the heart.

Witthauer gives the following conditions in which vibration massage is indicated:

1. In all kinds of weakened conditions of the heart in which it is working insufficiently.
2. In valvular disorders with disturbed compensation.

3. In hypertrophy and dilatation, idiopathic or secondary, when the heart muscle is insufficient for the increased work.
4. Light chronic myocarditis.
5. Adipose hearts.
6. Heart neuroses.

FIG. 8.—ZANDER APPARATUS TO OBTAIN THE EFFECT OF HORSEBACK RIDING.

It is contraindicated in arteriosclerosis and aneurysms.

In direct vibration the plate is first lightly placed on the neck, then gradually passing down over the ribs and sternum, especially over the regions of the larger veins, each treatment lasting 2-3 minutes.

By the indirect form of massage we mean massage of those parts of the body in which circulation is influenced, as in the abdomen; and general muscle massage in which a general cutaneous hyperemia is caused.

In stomach and intestinal disorders mechanical vibration is especially

valuable. In conditions in which there is a lessened HCl production, a long-continued vibration over the gastric region causes an increase in the flow with relief from the symptoms, after all medical and dietetic measures have failed. In dilatation and atony of the stomach a large percussing surface should be used, and the duration of the treatment should not be over five minutes, as longer treatments cause an excess in the secretion of HCl which is already usually increased in these conditions. With massage should go dietetic measures. The meals should be small and frequent, the bowels well regulated, and too much fluid avoided.

Witthauer has had exceptionally good results with vibratory massage in cases of floating kidney, especially when of a mild degree. He uses comparatively slow vibrations on the abdominal wall, then presses the plate over the kidney, and finally brings the plate in rapid swings over the region in order to cause contraction of the elastic elements in the neighborhood of the kidney and the abdominal walls; and the same movements are made over the back in the lumbar region, lasting about three minutes.

In gynecology the indications for mechanical vibratory massage are the same as for manual massage. It is contraindicated in all acute and subacute inflammatory processes, especially gonorrhea and in malignant growths. In parametritis, subinvolution of the uterus, and chronic metritis vibration of the abdominal wall is of value in the restoration of normal conditions. The men specializing in gynecology make use of vibration of the uterus directly for a number of conditions; for this purpose special apparatus and careful technique are necessary.

In neuralgia and other disorders of the sensory nerves very good results have been reported. In trigeminal neuralgia Hohnbaum reports that, in several cases, the pain in the part supplied by the supraorbital branch is diminished in a short time. He places the plate of the vibrator over the supraorbital foramen, uses moderate pressure, and gives a treatment lasting three to five minutes. In occipital neuralgia one places the vibratory plate over the neck muscles and over the foramina of exit of the nerves on both sides.

In sciatica the indications for vibration are marked, and better results are obtained, as a rule, in this disorder than in any other nervous trouble. In the acute stages rest is indicated. In the more chronic and subacute stages vibration over the tender points and over the pelvic and lumbar muscles is useful. Deep vibration with a small plate between the tuberosity of the ischium and the trochanter causes a preliminary pain sensation, which is succeeded by a feeling of relief. In addition to vibration, the movements of the legs, B 8, rotation, B 4, hip-knee extension, and B 2, extension of the hip, should be used.

In the hysterical pains and paralyses vibration massage has been used with good results. In the hysterical cramp of the esophagus and

pharynx, in the condition known as globus hystericus, vibration over the larynx and neck will frequently cut the paroxysm short. The psychic effect is undoubtedly the principal cause of this improvement.

In the rheumatic conditions and in the muscular atrophies following neuritis and non-use vibration massage probably has the same effect as does the manual form. The exudates in rheumatic joint conditions are probably more quickly influenced by vibratory massage than by manual. It can be more localized and the effect is not so superficial as in that form.

SUSPENSION

The use of the apparatus devised by Sayre for the suspension of the body, for the purpose of applying plaster casts in cases of tuberculosis of

Fig. 9.—Showing One Way of Applying Suspension.

the spine, has also been extended to other disorders. The action of this apparatus is to cause an expansion of the intervertebral discs and also a thinning of the nerve roots of the spinal nerves. In this way meningeal adhesions are broken up and meningeal thickenings are absorbed.

In applying suspension the patient may either stand or sit; the chin should be well padded, as severe pains in the jaws sometimes result when the chin-strap presses too severely. The weight to be applied varies according to the duration of the treatment. If it is very short the patient may be suspended so that his toes barely touch the floor; if of some minutes' duration a weight of from twenty to fifty pounds will be found to be quite sufficient. To determine the weight exactly a dynamometer should be placed above the hook on the cross bar. There are apparatus consisting only of the head and arm bands, and variable weights connected by a cord passing over a pulley. On this form the weights may be easily changed to suit conditions. The treatments at first should be of short duration, one to three minutes; later, when the weight is not too great, the duration may be extended to five or ten and sometimes even up to fifteen minutes.

While the patient is suspended, there is an increase in the blood pressure and pulse frequency, and sometimes a slight elevation of the temperature. After being suspended for some time the patients complain of pain in the jaw and teeth radiating upward, a feeling of pressure in the back of the head, vertigo and pain in the back.

The procedure is contraindicated in patients suffering from valvular heart disease, arteriosclerosis or myocarditis, pulmonary disorders, or myelitis. In those with acute or subacute inflammatory disease of the spinal meninges suspension may cause an increase in the symptoms and an extension of the process.

It has been of value in relieving the shooting pains in tabetics, and some authors report that the ataxia and general condition are also improved. Bogroff reported improvement in 216 of 289 cases of tabes treated by this method. In the early stages of tabes it is contraindicated, and may cause harm.

Lateral sclerosis, paralysis agitans, and sciatica are sometimes much improved by this treatment; while neurasthenia, traumatic neuroses, and insomnia are much benefited. The method has been used in a rather obscure group of cases, in which pain in the course of certain of the nerve trunks, especially those from the brachial plexus, is a prominent and usually the only symptom complained of. Radiographic studies of the vertebra seem to show that in these cases there is a narrowing of the intervertebral foramina; and it has been suggested that the pain is due to pressure on the nerve trunk—which might be relieved by suspension. Only a very small group of these cases have been so treated, but the results in these do not warrant the belief that the method will be of great value.

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CHAPTER VIII

ELECTROTHERAPEUTICS

William Benham Snow

The present-day consideration of electrotherapeutics views the subject from very different points of view from that of even a few years ago. Improvements in apparatus, technique, and the knowledge of physiological effects and therapeutic indications for the employment of the various electrical modalities or methods of application have given the subject a new impetus, placing it upon a substantial, scientific, and enduring basis.

There is so much of value in the consideration of methods of application, physiological action, and therapeutics that to consider the physics of electricity in the limited space allotted to the subject does not seem practicable. There are, however, a few terms in common use in electrotherapeutics which, to those not familiar with the subject, will require explanation.

Definition and Explanation of Terms.—Electricity has been variously considered during the years that its active properties have been understood. It has been left, however, for the latter day investigators, since the discovery of radium, to discover its true nature. It seems now to have been demonstrated to the satisfaction of modern investigators, though difficult to accept by many of the veteran workers, that it is composed of electrons which are actual substance. This was discovered when Sylvanus P. Thomson demonstrated that the atom of hydrogen had been resolved into a little more than 800 electrons. Oliver Lodge has since said that these electrons are "the substance of which matter is made."

Electricity has been defined by Professor Samuel Sheldon, of the Brooklyn Polytechnic, as "A material agency which, when in motion, exhibits magnetic, chemical, and thermal effects, and when at rest or in motion exerts a force upon other electricity. Recent investigations indicate that it is discrete or granular in nature, and there may be two kinds, namely, positive and negative."

The direction of the current has been shown, furthermore, to be in the opposite direction to that which it was believed to be by the early

observers, when it was said that the current passed from positive to negative. It is now clearly demonstrated that the negative electrons pass toward the positive in the cathode stream, and that the current flows in that direction. Furthermore, it is difficult to determine whether the electrons do not pass in both directions, i. e., toward each other—the negative toward the positive, and the positive toward the negative—as stated elsewhere in connection with the consideration of electrolysis. As one watches the discharges from the two opposite terminals of a Holtz machine in a darkened room, it would seem that the electrons are starting out from both poles, and that they were probably passing through the dark field between the two poles toward each other, in accordance with the laws of attraction by which oppositely charged bodies seek to approach each other, while like charged bodies are repellent to each other. We have here the suggestion of the passage of electrons from both terminals.

A definite consideration of the various properties of electricity which must constitute a thorough consideration of the subject must recognize three factors: (1) amperage or current strength; (2) voltage, also designated potential, or (E. M. F.) the pressure condition of the current, or its capacity to overcome resistance; and (3) resistance offered to the passage of the current. So we have Ohm's law: $C=\frac{V}{R}$. This formula may be transformed into various arrangements by transposition, according to the conditions to be considered. For instance, we may say that, if $C=\frac{V}{R}$, then $R=\frac{V}{C}$, etc. One law proven practical follows: When overcoming a given resistance, the heat produced varies as the square of the current; in other words, when acting through a resistance of one ohm, four times as much heat will be produced as by the passage of one (C^2R). We might give numerous laws of the physics of the relation of these formulæ. In a medical work, however, the writer does not see any special advantage to be obtained from the consideration of the higher mathematics as concerns electrical currents.

Voltage may be defined as the difference of electrical potential; the analogue of difference of pressure in hydrostatics or hydraulics.

Amperage.—Strength of the electrical current expressed in amperes.

Frequency.—The rate of oscillation of alternation in an alternating current circuit, in contradistinction to periodicity in the interruptions or regular variations of current in a direct current circuit.

Periodicity.—The rate of rise and fall or interruption of an unidirectional current, in contradistinction to the frequency of an alternating current.

Ohm's Law.—The strength of the current varies directly as the applied electromotive force, and inversely as the resistance of the circuit;

or, the current, expressed in amperes, equals the electromotive force, in volts, divided by the resistance in ohms ($C=\frac{V}{R}$).

Resistance.—The opposing influence of a body (solid, liquid, or gaseous) to the expenditure of electrical potential. It is expressed in ohms; one ohm of resistance will permit the flow of a current of one ampere as the result of a pressure of one volt. The effect of the expenditure of electrical energy in resistance is to make it appear as heat.

Watt.—The product of the voltage by the amperes. With a 110-volt current of 5 amperes we have 110 volts x 5 amperes equals 550 watts, or about 2/3 of an electrical horse power.

Following out the suggestions of these definitions, there are certain questions which arise. The nomenclature adopted a few years since by the engineers, and later by the American Electrotherapeutic Association, limited the term *"frequency"* to alternating currents or oscillatory currents, which may be represented as in Fig. 1.

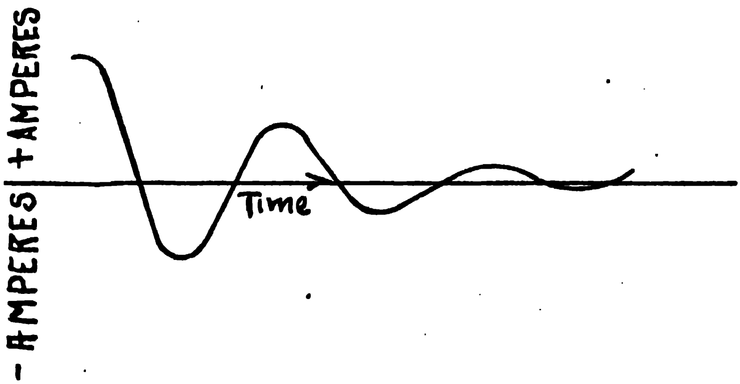

FIG. 1.—HIGH FREQUENCY OSCILLATION.

The term periodicity has been used to refer to the rate of interruption or make and break of a unidirectional current circuit. We therefore speak of a *current of high periodicity,* meaning that a rapidly interrupted current is passing in one direction. We speak of currents with reference to direction as *alternating and direct.*

Alternating currents may be of high frequency, and the waves or character of oscillation may vary markedly, according to the conditions of the circuit in which they are produced; from the uniform sine wave of the sinusoidal current, Fig. 2, to the wave in which the summit is largely on one side of the neutral line, as shown in Fig. 3. In the latter the current becomes very nearly directional in character, the lower curve representing the inverse or lag of the current, as of the current of the Ruhmkorff coil.

A pulsatory current is a directional current in which the waves have a recurrent rise and fall usually uniform.

There are various other differences in the characteristics of currents,

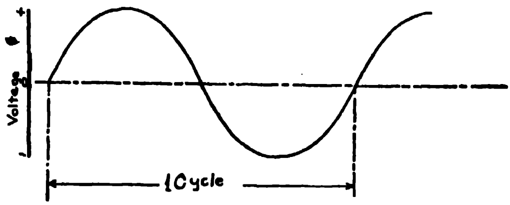

FIG. 2. SINUSOIDAL CURRENT.

depending upon the character of the make and break or interruption in the circuit. The current from the coarse wire Faradic battery would be indicated by Fig. 4, the lines of interruption are abrupt or sharp, and

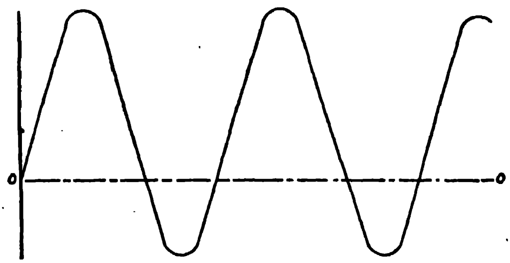

FIG. 3. RUHMKORFF COIL INVERSE.

the sensations produced with such a current are relatively painful, according to the frequency at which the alternations occur, the disagreeable effect being less as the frequency is more.

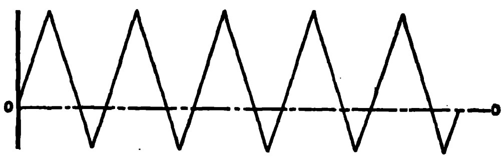

FIG. 4.

A high frequency current is an oscillating current in which the rate of oscillation is such that no perceptible tissue response is produced at approximately a rate of 10,000 per second. Above that rate the current produces only the effects arising from the passage of the electrons through the tissues.

The constant current may be defined as a current of uniform current strength flowing in one direction.

APPARATUS

Great changes have taken place in the types and features of construction of electrotherapeutic apparatus during recent years. The apparatus now in common use consists of the modern types of static machines, various X-ray coils and transformers of great capacity, and improved wall plates and transformers for employment with the constant current, besides various types of sinusoidal apparatus.

Static Machines.—The modern types of static machine comprise the Holtz, the Toepler-Holtz, and Wimshurst machines, which have varying advantages and disadvantages.

The Holtz machine, of which the Toepler-Holtz is a modern modification, probably possesses most general advantages for the specific use of the static current. The distinctive feature consists mainly in the arrangement of the stationary plates. Two long, narrow plates being placed above and below, separated by an air gap approximately four inches in width, which are placed between adjoining revolving plates. This arrangement insulates the two fields from each other by an air space, and increases the internal resistance of the machine, rendering it possible to produce at the spark-gap, under otherwise favorable conditions, a very long and steady spark discharge, as is required for the treatment of some conditions with the static current. That the current output of a Holtz machine is not quite so large under otherwise similar conditions as that of a Toepler-Holtz machine is another advantage when administering the current for its mechanical effects for the requisite twenty-minute period.

Coils and Transformers.—The discovery of the Roentgen ray, with the ever-increasing demands for rapid radiography, has tended to the production of very powerful types of Ruhmkorff coils—larger even than those required for long distance wireless telegraphy. These coils have occupied an important place for this purpose, until recent times, when the employment of the Lemp machines (Fig. 5) or interrupterless apparatus was introduced. This apparatus combines the rotary principle and takes from the alternating current apparatus the summit of the waves, accumulating on either side the opposite polarities, thereby producing a unidirectional current, getting rid of the objectionable inverse of the Ruhmkorff coil. These machines, with varying modifications, have been put upon the market by nearly all the manufacturers of X-ray apparatus.

This last type of transformer combines a rotary converter with a closed circuit transformer for raising the potential of the current, and produces unidirectional currents without lag or inverse, rendering them invaluable for X-ray and therapeutic purposes.

Another type of high frequency transformer has been manufactured

for producing fairly low potential currents of fairly high amperage, without reference to current direction. The object of this apparatus is the production of thermic effects upon the tissues, which has been designated by Nagelschmidt as "diathermic." This term, however, in the writer's judgment, is burdening therapeutics with another name which is not distinctive from a therapeutic point of view, as the thermic action of the current is for the induction of hyperemia, a d'Arsonval arrangement and solenoid always playing a part in the circuit.

Other types of high frequency apparatus have been devised, which are designated *Tesla* apparatus. These take the current from alternating

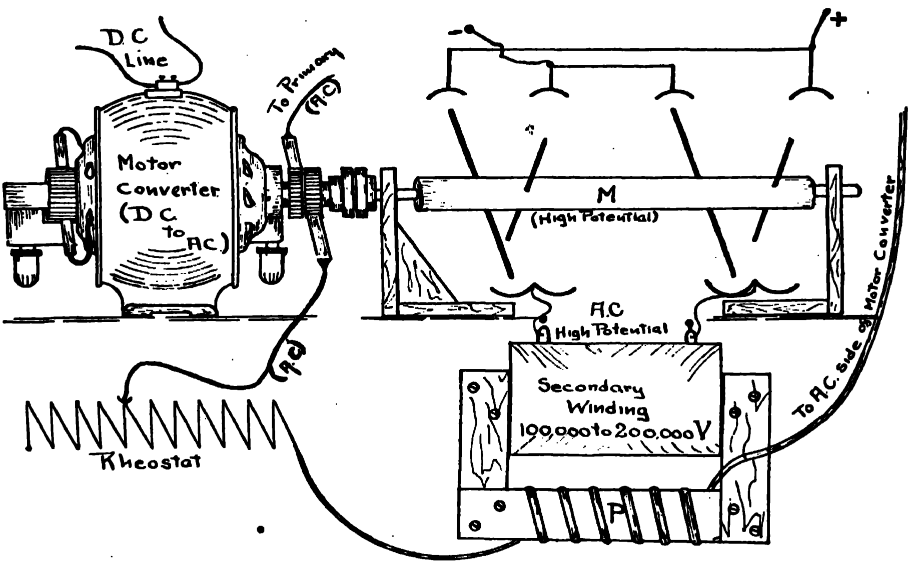

FIG. 5.—MODEL OF LEMP TRANSFORMER.

current sources, and, instead of transforming it into a direct current, require a rotary converter when the commercial current is direct. These transformers are manufactured both in the form of office cabinets and portable coils. While the current produced is not the same as that derived from unidirectional current apparatus, they do produce thermic effects of a satisfactory character, lower blood pressure, and are of practical utility with specially designed X-ray tubes for use with the X-ray, but are not designed to do rapid radiography. One advantage of these recently developed transformers over the Ruhmkorff coil is that they all dispense with an interrupter.

Interrupters have always been the greatest obstacle to successful work with the Ruhmkorff coil, either for producing the X-ray or high frequency currents; but latterly very perfect types of interrupters have been invented of the Wehnelt type, and also mechanical interrupters.

At the present time one great disadvantage is experienced by physicians in the tendency to the construction of commercial circuits of the alternating type throughout the country. This is particularly a disadvantage in the employment of the modern types of interrupterless transformers, except for the alternating current types of transformer referred to.

The motor dynamo, though a rather expensive part of an outfit, is almost indispensable for use in connection with these rapid radiographic devices for conversion of the alternating into the direct current. The motor dynamo comprises an alternating current motor operated on the same shaft with a direct current dynamo.

A resonator for high frequency transformation of the current consists of an arrangement of two Leyden jars connected with the primary sources of the current from any high potential source, static or transformer, placed in series with a spark-gap and provided with a d'Arsonval solenoid connecting the outer coatings of the two Leyden jars. The object of a resonator is the conversion of a current from a static machine, coil, or transformer into a high frequency current. To one side of the d'Arsonval solenoid may be connected one terminal of another solenoid or coil, for raising the potential or voltage of the current. From the other terminal a one-pole current may be administered. This current is known as the *Oudin current,* the object of which is to produce a discharge of high potential, giving off a long effleuve, or sparks. In therapeutics the Oudin current possesses very little advantage as a therapeutic measure, except for fulgeration; because these currents are better adapted to produce thermic effects, which requires a current of greater amperage and lower potential, as the d'Arsonval current. The special requirements for the administration of these various currents are shown in the parts of the chapter devoted to therapeutics.

Wall Plates.—*The constant current wall plate* may be used in connection with a series of galvanic cells, or from a direct current source, either from the commercial circuit or from a motor dynamo used for transforming the alternating to the direct current. It matters not for effect what is the source of the direct current—battery, commercial circuit, or transformer; for, in the modern type of apparatus, with the modern currents, the effects of the direct current are uniformly steady and constant as employed with the office wall plate.

Electrodes and other special devices will be considered in connection with demonstrations for their employment.

PHYSICAL EFFECTS OF ELECTRICITY

The physical effects of electricity which concern the physiologist and therapeutist are included in the three characteristic effects of electrical

currents, common to their action under otherwise favorable conditions, *viz.*, the electrolytic, mechanical, and thermic effects.

Electrolytic Effects.—Electrolysis is that property of an electrical current by which it effects the dissociation of ions or atoms with the formation of new chemical combinations in an electrolyte. In other words, the current produces electrical decomposition and ionization whereby the character of chemical substances is altered, and conveyed by the electrons in the direction of the current.

Electrolytic action is derived practically from the constant or direct current—a current of relatively large amperage and low potential or voltage, as applied in therapeutics.

Thermic Effects.—The thermic action of electricity is due generally to the passage of currents through tissues or substances which offer resistance to their passage. This is true of all currents to a degree relative to the current strength or amperage. The constant and high frequency currents are peculiarly active in this respect. In therapeutics the employment of the high frequency currents is preferred for producing heat in the tissues, because they do so without electrolytic action, whereas the constant current not alone heats the tissues, but produces a degree of chemical decomposition in its passage which may often be detrimental to the integrity of the tissues and their functions. Furthermore, high frequency currents in their passage through resistant bodies produce a degree of heat out of proportion to the current passing. This phenomenon is accounted for by the oscillatory character of the current, whereby the atoms are set in a state of very rapid vibration, another vibration which accentuates the heat vibrations.

Mechanical Effects.—The mechanical effects of electricity may be derived from all currents; for, wherever either of the previous effects, electrolytic or thermic, are produced, there is an increased cell activity, due to the passage of the electrons through the tissues; for these electrons, infinitesimal though they are, must be considered as matter passing through matter. These minute bodies pass in very great numbers. The substantial character of the electron must be always taken into consideration.

The *appreciable mechanical effects* are due to the influence of electrical currents under changes of potential—making and breaking the current—whereby muscular cell or tissue pulsations are induced, effecting mechanical movements which physically influence functional activities.

PHYSIOLOGICAL EFFECTS OF ELECTRICITY

The physiological effects of electricity, considered from the point of view of the three characteristic physical properties of the current, afford

a field rich in possibilities, inducing, as they do, definite physical responses in the organism, which are capable of producing marked structural changes and increased metabolism.

The study of the effects of electricity upon animal tissues is the study of reflex or responsive action to its stimulating influences.

The accidental discovery by Galvani of the response of muscular tissue to nervous stimulation led to the discovery of the constant current, which was for a long time, and is often now, designated as the *Galvanic current.*

Muscular Response to Nervous Irritation.—Whenever a nerve is stimulated, the muscular structures supplied by that nerve respond with contraction, when the nervous mechanism from center to periphery is in its integrity. This principle has been made use of diagnostically for the purpose of demonstrating existing conditions of the central and peripheral nervous system; and also for inducing exercise movements of the various muscles of the body, in conditions of paralysis, when the nerve and the cord centers were intact and responsive.

If the constant current is used for the purpose of stimulating muscular exercise, it is necessary that the application be made to the motor points, because the potential or voltage of this current is so low that it is not capable, except with strong currents, of passing through the skin and underlying tissues with sufficient energy except at those points where the nerve comes near the surface. *The resistance of the skin* is such that considerable current from a low potential source is necessary for the current to pass through it. Though the human body is practically a normal salt solution, the skin, with its dry exterior, offers resistance practically one hundred times greater than the *moist tissues* beneath. The fluids of the body are always the best conductors; hence the blood stream, venous and arterial, and the lymph channels offer the best media of conduction.

The *muscular structures* are distinctly better conductors than the nerves, which disproves the notion that the nerves are the usual conductors of electrical currents. On the contrary, they are the conductors of nervous impulses which are not electrical, but travel with far lower velocity than the electrical current.

That nervous impulses are not electrical is readily apprehended from the fact that the rate of conductivity of the nervous impulse is very slow compared with the lightning speed of electrical currents. The notion, often presumed, by those not informed, that the nervous system is a great electrical system is, therefore, readily disproved. The fact that the nerves are not the best conductors further strengthens the proof against this fallacy.

Currents of low voltage, as the constant and low volt-induced currents, are conducted by circuitous paths through the tissues, according to

the conductivity of the medium, always following the path of least resistance.

The *effect of local nerve stimulation* is due to the irritating or otherwise stimulating influence of the current where applied, and not because the current is passing along the path of the nerve. Other irritants practically stimulate muscular contractions, though differently, such as the applications of heat, flagellation, or the irritation of a nerve by an inflammatory process. If the current which excites a muscular spasm has a rate of interruption above 600 per minute, the spasm will be constant or continuous until the muscle is exhausted by fatigue.

In cases of neuritis or inflammation elsewhere, as in joints, the muscles are more or less in a condition of fixed contraction, resulting in pain and stiffness. This arises from nerve irritation as from blood stasis, and, like stasis, adds to the symptom-complex of a vicious circle, and is not, as has been often said, "Nature's method of cure."

To induce contraction it is not necessary that the static sparks and other slowly interrupted high potential static modalities be applied to motor points, because the high potential currents penetrate readily and cause contraction wherever applied, either of the muscle cell, the nerve or its branches, irrespective of motor points. The currents of high frequency do not produce muscular contraction, which is the distinctive feature of these currents.

The constant current and the induced or Faradic current of low voltage produce burning or stinging or irritating effects when applied to the skin. This effect chiefly accounts for the responses induced in this way; whereas, when the static current flows without interruption into the tissues, it produces no sensation—no irritation and no perceptible contraction. Interruption with changes of potential in the circuit is a prerequisite to the induction of contraction with the static current.

The high frequency currents of high potential, when the rate of interruption exceeds 10,000 per second, produce no perceptible nerve or muscle response, because the tissues are incapable of responding perceptibly to that rate of interruption.

Independent Irritability.—Muscle cells respond independently of the nervous system. "Under normal conditions in the body," as stated by Howell, "a muscle is made to contract by a stimulus received from the central nervous system through its motor nerve. If the latter is severed, the muscle is paralyzed. We owe to Haller the proof that a muscle thus isolated can still be made to contract by an artificial stimulus—e. g., an electrical shock—applied directly to it. . . . In a number of ways, however, physiologists have found that the muscle substance can be made to contract by a stimulus applied directly to it, and, therefore, exhibits what is known as independent irritability. The term irritability, according to modern usage, means that a tissue can be made

to exhibit its peculiar form of functional activity when stimulated—e. g., a muscle cell will contract, a gland cell will secrete, etc.—and independent irritability, in the case under consideration, means simply that the muscle gives its reaction of contraction when artificial stimuli are applied directly to its substance. This conception of irritability was first introduced by Francis Glisson (1597-1677), a celebrated English physician.

"A simple proof of the independent irritability of a striated muscle is obtained by cutting the motor nerve going to it and stimulating the muscle after several days. We know now that in the course of several days the severed nerve fibers degenerate completely down to their terminations in the muscle fibers, and the muscle, thus freed from its nerve fibers by the process of degeneration, can still be made to contract by an artificial stimulus. . . . Direct stimulation of the muscle substance, on the contrary, causes a contraction. We are justified, therefore, in saying that skeletal muscle possesses the properties of independent contractility (Haller) and independent irritability (Bernard). By the former term we mean that the shortening of the muscle is due to active processes developed in its own tissue, by the latter we mean that the muscular tissue may be made to enter into contraction by artificial stimuli applied directly to its own substance. This latter property cannot be said to hold for all the tissues. Whether a nerve cell or a gland cell may be made to enter into its specific form of activity by the direct application of an artificial stimulus is still an undetermined question."

These observations that we have quoted are valuable as showing that cells contract in their protoplasmic structures independent of nervous stimuli.

The failure of the low potential currents to produce contraction when applied to the skin, except directly to the motor points, is due to the resistance of the skin and underlying tissues. The contractions that may take place with such currents, therefore, do not directly affect the muscle cell.

The observations are valuable, however, as indicating the effects of high potential currents, which pass readily through the skin and are diffused throughout muscular tissue, whereby the volume of the muscle, independent of the nerve supply beneath and surrounding an electrode, is induced to contract *en masse* relative to the potential of the current discharged, if the interruptions are lower than 10,000 per second. Rhythmical contraction of the muscular mass, with intervening release, takes place if the contractions are below 600 per minute or 10 per second. Six hundred interruptions per minute is the limit at which a period of release will intervene between periods of contraction. The rate of interruption most agreeable, and at the same time most efficient, is between 120 and 200 per minute. Above 600 per minute muscular spasm with

tonic contraction persists up to 10,000 per second, when all contraction ceases. The recognition of these principles of tissue response is of great importance as effecting physiologically valuable results from the employment of the currents which, by the induction of rhythmical activity, induce or effect local metabolism and tissue drainage, the employment of which in therapeutics will be subsequently considered at length.

Determining Characteristics of Electrical Currents.—In order to consider more definitely the effects of the electrical modalities, there are certain characteristics of the various electrical currents which determine their character of action, whether *electrolytic, mechanical, or thermic.*

Constant Current.—The constant current—until the present nomenclature was adopted by American and European engineers known as the Galvanic current—when compared with the static and high frequency currents, is a current of relatively large amperage and low potential, the voltages usually employed in therapeutics ranging from 100 to 120 volts, and the amperage from 1 to 1,000 milliamperes, according to the indications. This current may also be employed interruptedly, when successive contractions are induced, in effect relative to the quantity and voltage of the current employed, varying with the tissues which it penetrates as to the force or presence of contractions.

The *physiological actions* of the constant current are largely thermic and electrolytic; the mechanical action, which is energetic under favorable conditions, being of secondary importance in its therapeutic employment, other currents serving more practical indications for that purpose.

The *currents or modalities from the static machine,* which is also a constant current, are of relatively very high voltage, and from Holtz machines of very small amperage, approximately an average amperage of from 1/4 to 1 milliampere, varying with the number of revolving plates and the speed of the machine; and a voltage of from 100,000 to 800,000. The effects of the static current when *not interrupted* are practically nil, the current flow being so small that thermic effects are inconsiderable, and the electrolysis is practically nothing, and the perceptible mechanical effects are absent. On the other hand, if this high potential current *is interrupted* and regulated to a rate of interruption below 600 per minute, it produces more marked contractions and with less annoyance or irritation than currents from any other electrical source. In the resulting mechanical effects upon the tissues, the static current, when regulated and properly administered, is capable of producing successive contractions of the cells individually and of the cells *en masse,* thereby expressing the infiltration, when present in indurated tissues, and otherwise affecting metabolism.

Induced Current.—The currents as produced by the *Ruhmkorff coils,* when of very slow rate of interruption, are capable of producing

similar effects of tissue drainage by the induction of muscular contraction, but in no sense duplicate in scope or control the static currents, and are more disagreeable to the patient.

The current from the *large coils*, which are constructed for use with the Roentgen ray, are provided with current-breaking devices, which interrupt the current at a very rapid rate. The currents from these coils produce a stinging, cauterant effect, devoid of the characteristic type of contractions produced by the static current.

Sinusoidal Current.—The sinusoidal current, alternating in character, produces no electrolytic effect, because the alternations, changing the polarity in equal quantities, neutralize each other. The effects of this current are principally mechanical, and, to a degree, thermic, but in neither of these actions are they so effective, either as to the thermic effects produced with the high frequency d'Arsonval current, or the mechanical effects of the static current. There are, hence, few, if any, conditions in which this current excels the other currents in therapeutics. It is very useful, however, to the physician in too small quarters to have place for a static machine.

High Frequency Current.—The high frequency currents, the most efficient of which is the d'Arsonval current, produce no electrolytic effect whatever. This is demonstrated by placing the opposite poles in a solution of iodid of potash, and passing a large current through the solution, when no decomposition takes place, as would be indicated by change in color in the solution.

The *thermic effects* of the high frequency currents are more marked than from any other source of electrical energy. This heat-forming action is in excess of the actual effect that would be derived from a constant current of the same current strength. The thermic action is derived both from the resistance to the current and the effects of high frequency oscillation upon the tissues or other substances through which it passes. The direct d'Arsonval current (see Fig. 6) is the high frequency current usually chosen for the induction of thermic effects.

The *physiological effect* upon the tissues through which the current passes between two electrodes placed upon opposing surfaces is derived from the increased blood supply through the tissues, a natural provision to maintain an equilibrium of temperature and prevent burning of the tissues. In other words, hyperemia is induced by heat in the path of the current, and may be carried to a marked degree, when it will persist with its beneficial effects for a long time. Applied in this manner, the beneficial effects of local hyperemia are induced upon the tissues. These will be given full consideration in following pages.

The *mechanical effect* of the high frequency current upon cell structures is due both to the thermic action, which increases the activities of the tissues through the mechanical actions derived from the increased

rapidity and volume of the blood stream, and also to the passage to and fro through the tissues of the active electrons as previously described in connection with the mechanical actions of the passage of the electrons with the static current. It is this action that accounts for the distinctive

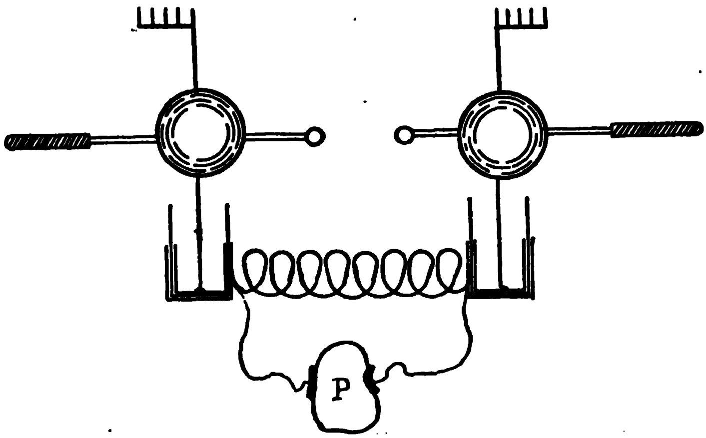

FIG. 6.

effects upon metabolism and the actual relaxation with lowering of blood pressure.

The *physiological effects* of other currents resemble the effects of the important modalities, variations existing only in degree.

Basis for Physiological Effects.—The three distinct effects of electrical currents, as described under physical effects of currents—(1) the electrolytic, (2) mechanical, (3) thermic—practically include the important actions of electrical currents to which the physiological studies must be referred.

MECHANICAL EFFECTS.—The mechanical effects, as previously shown, are due to the *excitomotor* influences of nerve and cell stimulation—sensible effects—and otherwise the insensible effects arising from the passage of the electrons through the tissues. The demonstration of the substantial character of the electrons indicates the certainty of mechanical action effected by their passage in great numbers through the tissues, i. e., these millions of small bodies coming in contact with the structures of the cells affect them mechanically.

The mechanical effects of electrical currents may, therefore, be properly divided into the gross or sensible effects which are the local effects, at the site where the current passes in or out, or, as in the case of the static wave current, in *and* out of the tissues, and (2) to the effects due to the passage through the tissues of the electrons, and (3) another undoubted effect: that of polarization, whereby certain other cellular movements are induced when bodies are like charged.

The *perceptible* mechanical effects of electrical currents are induced by make and break of contact with the tissues, as by the administration of sparks or convective discharges, or by interrupting the current in the circuit when the electrodes are in contact with the skin. These effects are associated with muscular contraction, and the contraction of other cells which respond to electrical stimulation, as of the yellow elastic tissues, by direct contraction of the tissues, or contractions induced by nerve stimulation, as by the application of electrical currents to motor points, or indirectly to the nerve trunks or branches.

The Static Current.—The static current, administered from one side of a static machine in the form of sparks or other modalities, induces the characteristic effects relative to the conditions of the circuit. Grounding one side of a static machine when the other side is connected by suitable electrodes to a patient, and sparks are discharging between the terminal balls at the spark-gap, or when a spark is discharged between a patient and a sparking ball which is connected to another grounding chain, very greatly accentuates or intensifies the effect of tissue contraction. The mechanical effects of electricity as applied in therapeutics are vastly more effective from the static current when scientifically employed than from any other current source.

The current from *high tension faradic coils* with slow interruptions is capable of inducing definite local contraction of a similar character, but only to a very moderate degree and to a limited area, when compared with the static modalities, and is not locally effective except by the employment of very small electrodes. It is consequently not practically applicable for the *general* employment of electricity, or *locally* to meet other than very moderate mechanical requirements. The induced current is, therefore, of very little practical use in the office of the physician provided with a static machine which is capable of giving every range of effect, from the most gentle required to the most profound effects produced by any other mechanical measure.

The static current has four distinct characteristics, which indicate its employment generally for the mechanical application of electricity. The qualities which give this current its prestige over other currents are: (1) great diffusion, (2) great potential, (3) unipolarity, and (4) the fact that it passes rapidly through to surround the capacities charged.

The diffusion of the static current is remarkably evidenced by the rising of the hairs, not only upon the head and body of the patient seated upon the insulated platform, but a sensation of similar effects is appreciable by other persons in the room. No other current passes over or through wooden substance as the static current does, nor through the air to be appreciably felt, nor by spark discharge under charges of small amperage and high potential, as the static current does. This remarkable quality of diffusion gives this current one of its most important and dis-

tinctive qualities, and largely explains the remarkable mechanical qualities of the current upon the tissues.

The great potential exceeds in this particular the practical possibilities of currents from other sources, for no other current can be delivered in so small quantity as the static current, combined with so great potential.

The Unipolarity.—In other words, this current is possessed of a directional quality from each pole, which, under great voltage, is seeking from both terminals to meet, when conversion of energy takes place, and the electrical charge is no more.

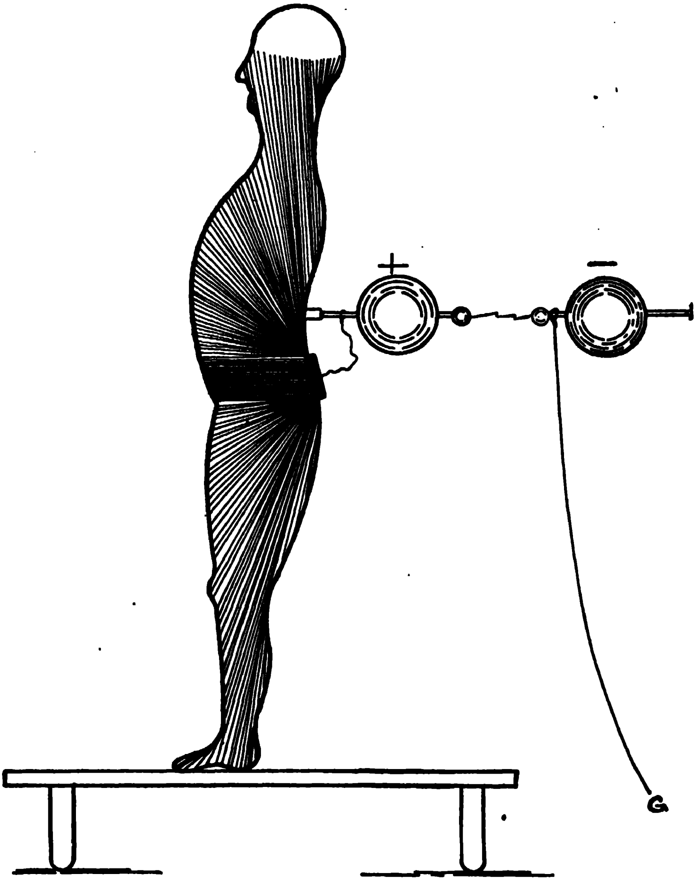

FIG. 7. GRAPHIC ILLUSTRATION OF THE ARRANGEMENT AND COURSE OF FLOW OF THE STATIC WAVE CURRENT.

No current better illustrates the physical principle that electricity is immediately produced and immediately dissipated than the static current. It is undoubtedly the unipolar character of this current, that causes the affinities to be so strong for the opposite polarity, that largely ac-

counts for the mechanical action of the current upon animal cells. It is the effort under potential of attraction of the electrons of two opposite charges to come together.

The static current, therefore, which has the property of staying for limited periods of time in a state of charge within the Leyden jar, and upon insulated surfaces, as in the static machine, is kinetic, and in movement the most active and energetic in its changes of position of all electrical currents. The significance of these qualities in therapeutics must be fully recognized to be appreciated. The characteristic qualities of the static current with the different modalities effect most energetic mechanical effects, the respective modalities varying in their indications.

The static wave current (Fig. 7) is the most valuable of the static modalities in its wide field of indication for the treatment of non-infected inflammation and its consequences, and for its effects upon general metabolism.

METHODS AND PRINCIPLES OF APPLYING ELECTRICAL CURRENTS

The therapeutic indications given in the preceding paragraphs suggest the employment of numerous methods, involving three distinct principles of action of electrical currents—electrolytic, mechanical, and thermic.

Electromechanical Methods

The electromechanical methods include the important static modalities, the wave current, vacuum tube wave current, static induced current, sparks, brush discharge, spray, pulsatory Oudin current of deKraft, sinusoidal current variously administered, and the induced current previously known as the Faradic current.

The Static Wave Current

The important features of this modality, or mode of application, are: (1) the grounding of the negative pole of the machine, (2) the spark-gap or distance between the terminal balls of the discharging rods, (3) the size of the terminal balls, (4) the rate of spark discharge at the spark-gap, (5) the regulation of the rate of spark discharge at the spark-gap, (6) the insulated platform, (7) the adjustment of a proper metal electrode applied directly to the skin or internal mucous cavities and connected to the positive side of the machine, and (8) the duration of treatment.

The above features of arrangement and control of dosage are of the utmost importance for the successful administration of this most valu-

able of electrical modalities. So important are they in the correct understanding of the details of administration, that a full understanding of each principle is essential to an accurate and successful technique.

1. **The Grounding.**—The grounding, as in the employment of all static modalities, except the static induced current, is an essential feature, because thereby the intensity of the effect is accentuated many times. A metallic connection must be made for this purpose directly from the negative pole of the machine by a wire or chain to some direct or unbroken metallic path to moist earth, as a steam radiator or water pipe.

2. **The Spark-gap.**—The spark-gap or space between the terminal balls of the discharging rods (see Fig. 7) determines the penetrating effect of the current employed. When the current is used in the treatment of a painful condition, or to relax a muscle in a state of spasm or tension, the spark-gap should be gradually lengthened as the toleration of the patient will permit, thereby gradually affecting the tissues to a greater depth, as the superficial muscular layers become relaxed or the infiltrating material is superficially expressed. The spark-gap when regulated, together with the adjustment of the size of the terminal balls, and the rate of discharge, is an accurate measurement of dosage—as accurate as any measurement in milliamperes of any other current. The dosage should always be designated in terms of spark-length, size of terminal balls, and rate of discharge—the three essential elements of dosage of this valuable modality.

3. **The Size of the Terminal Balls.**—The size of the balls screwed on the ends of the discharging rods determines the volume of the discharge. The smaller terminal balls give a greater current condensation, whereas as the size is larger it becomes greater, and with the same charge the current condensation is less and a much greater charge is necessary to overcome the same length of spark-gap. When the current breaks down the dielectric and passes across the gap from a large-sized ball, the current that has been stored up against the resistance produces a more potent discharge, which is always relative to the size of the terminal ball from which it is discharged. On this principle it is possible to regulate not only the amplitude or intensity of the current by the spark-gap, but also its volume or quantity. There should be, therefore, three or four sizes of terminal balls for operating the current with varying force, according to the conditions treated—respectively, ½ inch, ¾ inch, 1 inch, and 1½ inches in diameter.

4. **The Rate of Discharge.**—The proper rate of discharge is a prerequisite to a successful technique, as suggested in previous pages. For its therapeutic effects in the treatment of inflammatory conditions, for the removal of exudation, and to relax muscular spasm, the rate of interruption should not exceed 300 per minute. If the rate of discharge is less than 100 to 120, the intensity of the contractions are rather dis-

agreeable to the patient. A rate of 100 to 120 per minute, however, becomes very agreeable. The choice of rate, therefore, for the best therapeutic effects is between 120 and 300 per minute, being both more agreeable and more efficient.

5. **Speed Control.**—The speed control or rate of revolution of the static machine is of the utmost importance in order to regulate the rate of discharge to the varying spark-lengths. With the direct commercial current, a speed controller or rheostat having from 50 to 100 points, or even more, gives a sliding scale of varying resistance, which is capable of controlling the rate of spark discharge satisfactorily. Whenever the spark-length is increased, a change of resistance by the speed control will determine the rate of revolution, and thereby maintain a uniform spark rate. *With water power* the control of the speed of the water motor by regulation at the water cock of the volume flowing is one of the most effective methods of speed control. When the alternating current is the source of power, the employment of a mechanical speed controller gives a good control, but requires a little additional power to overcome the extra resistance of the apparatus.

One of the most important principles in the technique of manipulating the static wave current is the regulation of the rate of discharge at the spark-gap as effected by accurate control of the speed of the machine, and there is no point in which the average operator is apt to be more deficient, and none which some manufacturers seem oftener to neglect.

6. **Insulated Platform.**—The insulated platform is an essential to the successful administration of the static wave current. This modality has been compared to the charging and discharging of a Leyden jar, the legs of the platform representing the glass walls of the jar, and the patient the inner coating of the condenser, and the walls and floor of the room the outer coating of the jar. The comparison is in every way true, the current passage being directly to charge and discharge the patient with the electrical current, as the Leyden jar is charged and discharged when the current is passing into the Leyden jar with the spark-gap opened.

7. **Electrodes.**—The electrodes employed for administering the static wave current are preferably of metal. If sponges or other materials are used, they must be entirely saturated with a salt solution, or sparks will pass through the material to the patient, making the method very disagreeable. The same is true of the administration of the static-induced current. These metal electrodes are usually applied to the surface of the body always next to the skin, and are best made of a flexible metal, approximately 22 gage in thickness. A bottle cap composition is less expensive and more durable than block tin for these electrodes. This material may be cut with shears into sizes and shapes adaptable to the surface of the body. So also metal electrodes are made of various sizes to

conform to internal parts to be treated. These various electrodes are shown in illustrations referring to the regions where they are applied.

8. Duration of Treatments.—In the employment of this current it has been found by systematic study of the relative effects that twenty minutes gives the best average result. More than twenty minutes will often fatigue the tissues, whereas, when continued for twenty minutes, the current effects the most efficient drainage or expulsion of infiltration from the tissue without causing fatigue. Often ten to fifteen minutes is as long as is necessary to relax conditions of muscular cramp or spasm. Otherwise the usual dosage of twenty minutes will obtain the best average results. During a course of routine treatment the administrations should be given daily at first, and later on alternate days, until the patient is discharged.

The Vacuum Tube Wave Current

The vacuum tube wave current is employed under practically the same conditions of arrangement and control as the wave current, the only difference being that the vacuum tube is employed as an electrode. The advantages of this modality in certain cases are twofold: (1) the ease with which electrodes are formed by the glass blowers for adaptation to the various cavities of the body, and (2) that the vacuum tube discharges from the surface of the glass are moderately antiseptic, and produce certain local effects favorable to the destruction of germs in the superficial tissues. The disadvantage of this current is that the effect is not so positive and marked in relieving the infiltration as when the metal electrodes are used.

This current may be administered from either the negative or positive side of the machine. Where an infectious element is largely to be considered, the negative pole produces a larger degree of antiseptic effect, for two reasons: (1) that the cathode stream to a moderate degree produces X-ray effects when employed with vacuum electrodes, which are insulated where they pass through the orifice, and (2) that the chemical effect at the surface of the glass is greatest when the negative pole is inserted in the cavities. The mechanical effect, however, is most marked when applied from the positive pole.

The Static Induced Current

The static induced current, the first of the high frequency currents, discovered by Dr. Wm. J. Morton, is administered as a two-pole current from the outer surfaces of the two Leyden jars connected as shown in Fig. 8.

The *local mechanical effects* of this current are practically the same

as from the static wave current. The passage of the current, however, is by the shortest route through the interpolar tissues, making the local

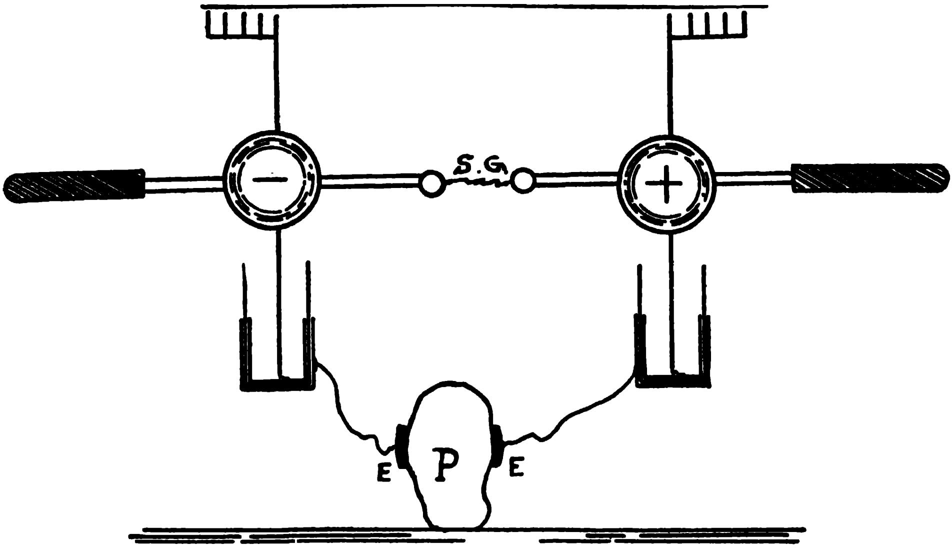

FIG. 8.—STATIC INDUCED CURRENT.

effect the only valuable effect of the modality, unless administered with numerous electrodes connected in series; whereas, the wave current passes from the surface of the electrode to the surface of the patient, and back through most of the tissues of the patient, with each charge and discharge of the current. The local effects of the current are mechanical at the two surfaces where the electrodes are in contact, but are devoid of the tonic effects of the wave current. It is indicated for administration to two parts of the body, both requiring energetic local treatment; as to the two knees or other large joints, the seat of some form of arthritis, or in cases of constipation due to obstructing conditions, as prostatitis, spasm at the sigmoid, or uterine retroversion, when one electrode may be applied in the rectum, and the other over the abdomen. Many other conditions may arise from time to time for the use of this current for the treatment of local infiltration. The greatest field of utility, however, for the static induced current will always be found in exercising the muscles in the treatment of obesity, anterior poliomyelitis, and for other motor defects. The methods of employing the current will be fully considered in the treatment of these conditions.

The Static Spark

This modality is designated a disruptive discharge. The principle of action depends upon the charging of the patient when seated upon the

platform as a Leyden jar is charged, then the discharge is drawn from his body with a metal ball connected with the earth (see Fig. 9) or to the

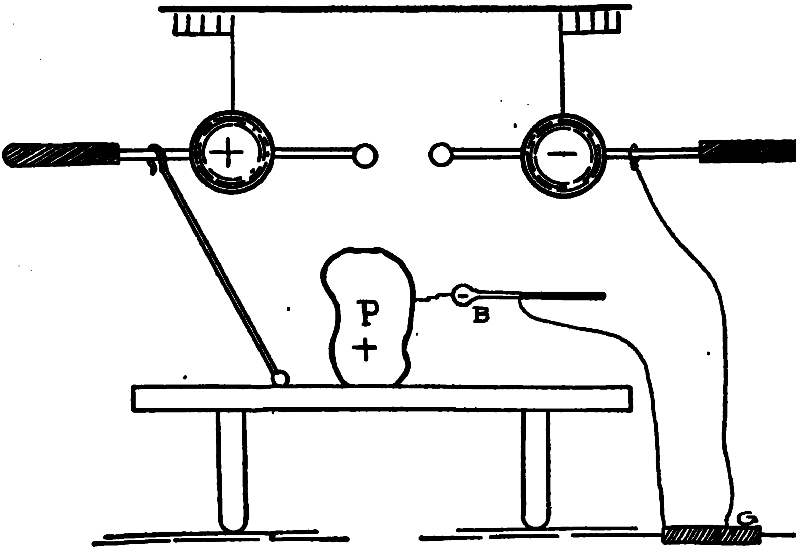

FIG. 9. STATIC INDIRECT SPARK.

opposite pole of the machine. The two methods of applying the static sparks are the direct and indirect.

For administering the direct method the patient is connected to one side of the machine, and the spark is applied by a direct connection of the sparking ball to the other side of the machine. This method is neither so effective, practical, nor convenient as the indirect method, as shown in Fig. 9. The grounding of the machine, as with the static wave current, is attached by most operators to the negative pole of the machine, and the positive pole is connected by a rod or so-called shepherd's crook to the platform, usually to a small metal plate placed beneath the chair, but at such a distance that sparks will not jump to the heels of the patient. Such metal plate should be approximately 12 or 14 inches square, and serves as a condenser, whereby, after discharging the patient, the recharge more promptly takes place, facilitating a more rapid succession of sparks when so desired.

An operating chain, provided with a direct ground connection, is essential for the administration of the indirect static spark. This should be connected to a convenient place opposite the platform, to a screw eye from which a wire is carried to a radiator or water pipe or to a rod driven into moist earth.

In administering the static sparks the operating chain connected with the earth should be held in the hands of the operator by the side of the

handle, in order that it will not be swinging about, and carelessly come in contact with the patient. Grounded in this way, the operator feels no effect of the current if the grounding is perfect. If, however, the ground connection is imperfect, there will be contraction of the wrists of the operator at each spark discharge during the administration to the patient. This will prove a practical method of testing the grounding. The regulation of the spark-length during the administration may be accomplished in two ways: (1) by controlling the speed of the machine, as described in the treatment by the static wave current, and (2) by allowing a spark to pass between the balls of the discharging rods during the administration. This latter method, though noisy, will control the length of the spark by allowing the spark to discharge at the spark-gap to be a little longer than the desired spark-length to be administered. For administering sparks, the best type of electrode is the one designed by the author, the so-called pear-shaped ball which adapts it to the employment of friction sparks by running the electrode over the clothing, the concave side of the ball conforming to the rounded form of the limbs and body of the patient. The spark should be administered with a wrist movement, the operator carefully measuring the distance during the application at which the spark will pass, or moving the ball across the part back and forth, at such a distance that but one spark will pass. Nothing is more annoying and disagreeable to the patient receiving spark administrations than the passage in rapid succession of two or more sparks during the administration. The sparks should be applied at equally measured intervals at which the patient will be expecting them; otherwise the patient is on and off his guard, when the physical and mental effects are not so good. Another method of administering the sparks, particularly valuable in treating contracted muscles, is by passing the ball with the machine running fairly fast parallel to the body, when in rapid succession sparks will pass along the course of the ball so passed. These have been called running sparks.

To definitely locate sparks in clefts and cavities the writer has designed a spark director, the ball or disc on the end of which is placed on the spot upon which the effect is to be produced, and the spark is applied to the metal ring. The effect is the same as if the spark were applied directly to the surface. The chain holder furnished with outfits answers for this purpose.

The *indications* for the use of sparks will be suggested under "Therapeutic Indications."

Friction sparks are applied by rubbing the metal part of the shank of the sparking ball over the clothing, or some fabric the thickness of which determines the length of the numerous short sparks which pass.

The *physical effects* of sparks by inducing intense contractions are to force elimination of exudation and infiltration and to relax muscular

spasm. For these purposes it is one of the most valuable modalities, and one often neglected by timid operators who have not sufficient tact to overcome the prejudices of their patients. The way to overcome this prejudice is to apply well-directed sparks to painful areas, and then ask the patient to move the part, when they will in most cases note marked relief from tension and pain, and ask for them rather than make further protestations against their employment.

The Static Brush Discharge

This modality is one of the most valuable in therapeutics, and partakes of the combined effects of a disruptive or spark discharge and a convective or effleuve discharge. It has for this reason been designated by Humphris a disruptoconvective discharge, which aptly describes its effect.

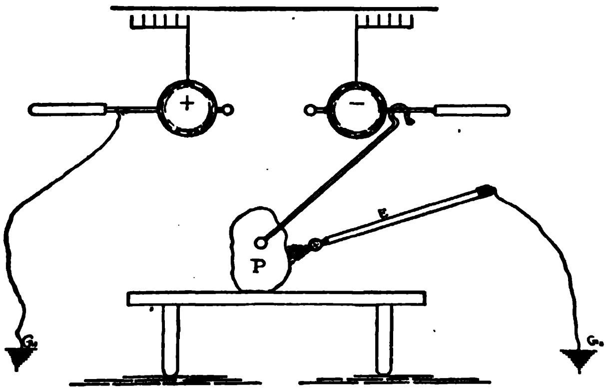

FIG. 10.—STATIC BRUSH DISCHARGE.
E, electrode to be held by operator. G_1 and G_2, groundings.

The arrangement for its administration is shown in Fig. 10. It will be noted that with this modality the positive pole is grounded. Experience has many times demonstrated the choice, as the discharge when the negative is grounded is stinging and disagreeable, and, furthermore, the relief from the treatment is but temporary. The administration is usually made with the electrode connected to another grounding, as with sparks. When, however, a mild effect is sought, the current may be passed through the operator or with the machine running at slower speed. In the administration of this modality it is imperative that the balls of the discharging rods be widely separated and that the machine be running at a rate of speed which will not cause sparking within the case. Otherwise, if a spark pass across the gap or within the machine, the patient will sustain a disagreeable contraction of the wrist; for, in order to administer this current efficiently, it is customary for the patient to hold the shepherd's crook in his hands during the administration. With this modality,

as with sparks and the wave current, the patient is insulated, and seated directly opposite the side of the machine to which he is attached.

The *electrodes* employed with the brush discharge are peculiar to this type of administration. They should be made of material which offers considerable resistance, but permitting the passage of the current. Wooden electrodes, when of a proper degree of moisture, are effective for the administration of the static brush discharge.

A new electrode consisting of a glass tube filled with glycerin, and provided at the end with a wooden ball or point terminal, as designed by Dr. Neely, serves as an excellent means for employing the brush discharge if the terminal ball does not become soaked with glycerin. To obviate this it is desirable that the terminal ball be removable; in other words, that it be made adjustable with a pin adapted to a hole in the terminal end of the glycerin-filled tube. The discharge from this electrode when in proper condition is very smooth, even, and effective.

The intensity of the brush discharge may be regulated by varying the speed of the machine, varying the dampness of the wooden electrodes, or by passing off the current through the operator.

The *indications* for this modality are given under "Therapeutic Indications."

The Static Spray

The static spray, a convective discharge or effleuve, is administered from single or multiple metallic points, held at a distance at which the spark will not pass to the patient. This modality has often been used for the removal of local pain, as the static brush discharge is used, and would be valuable if it were not that the latter modality is superior for that purpose.

As a *suggestive measure,* the spray applied as above is one of the most efficient and potent in therapeutics; for the stinging sensation when the brush is rapidly moved over and around the patient produces a very stimulating effect in the skin, which is calculated to impress the mind of the patient. The *method of administration* of the static spray is practically the same as of the brush discharge, except that it is usually applied with the negative instead of the positive grounding. It may or may not be administered from the second ground chain, depending upon the intensity of the effect desired under varying conditions of output or demand.

Under *slight variations,* this method is administered under the designation of the static breeze or static insulation, when the patient is seated upon a static platform with a brass, so-called, crown suspended over the head. This method is more spectacular than efficacious, as compared with the administration of the static wave current, which produces to a marked degree both local and constitutional effects. A danger from

the administration of the current in this way, with a breeze from the crown over the head, exists in that thick folds of hair or celluloid combs may be ignited. If, however, this modality is to be administered, the patient's hair, if a woman, should be braided and hanging down the back with the pins removed. It may sometimes be desirable to give this form of administration to very feeble patients, but in no cases is it a substitute in its effects upon metabolism and nutrition for the static wave current.

The Pulsatory Oudin Current of deKraft

This modality is administered from a specially constructed resonator provided with very large condensers (Leyden jars), in which the d'Arsonval is insulated from a secondary connection or so-called Tesla coil, to which is connected a long solenoid for the Oudin current. The pulsatory discharge is administered either from a ring electrode or other electrode held in the hands of the operator, at a distance from the patient.

When administering this modality one side of the resonator should be grounded, and a flat metal electrode be placed next to the skin upon the back or elsewhere, and connected to the ground. The administration should then be made with the discharging electrode in the hands of the operator, or suspended or sustained by an adjustable holder. The combination gives a rhythmical pulsatory discharge synchronous with the sparking in the resonator. This modality produces distinct tissue pulsations over the regions to which it is applied, effecting tissue drainage and at the same time stimulating metabolism in an effective manner.

The Sinusoidal Current

The sinusoidal current is an alternating current in which "the current flows periodically in opposite directions, and in both directions for the same length of time." The current is produced by the passage of a constant current through an alternating current transformer. The transitions from higher to lower potential with the alternation from negative to positive are so gradual with this current when the sine waves are not abrupt (Fig. 2) that very little perceptible mechanical effect is induced. The current, however, is of fairly large amperage, and the consequent stimulating effects are nutritional; owing to the mechanical effects upon the cells and the hyperemia produced. This effect, however, is not so marked as from the thermic action of the direct d'Arsonval current.

The *mechanical action* with this current, when produced in the form of abrupt transitions, with a current known as the *multiplex sinusoidal current,* are remarkable. This current (Fig. 11) is capable of causing deep and fairly diffused contractions of the musculature with no other

interruption than the surging of the current. While this current probably does not produce the degree of protoplasmic contraction of the static current, i. e., judging from the results, its mechanical actions are remarkably efficient in producing muscular exercise, as of the abdominal muscles

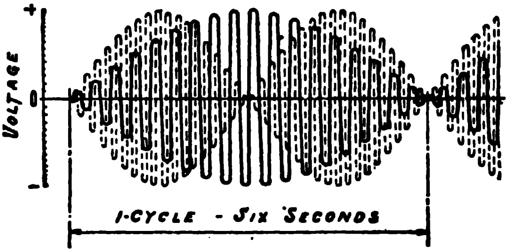

FIG. 11.

and intestinal tract. The method of administering this current may be stabile or labile. The multiplex current produces rhythmical contractions, which may be regulated in frequency without removal or change of position of the electrodes. It is often an advantage, however, to move about an electrode held in the hand of the operator, as over the abdomen in the treatment of constipation or pelvic or gastric atony.

The *indications* for the employment of this current are given under "Therapeutic Indications."

The Induced Current

Properly speaking, we designate what has been termed in the literature the Faradic current as the induced current. Any current derived from another current by means of either magnetic induction or static induction is an induced current. The static current so produced is designated as the static-induced current, whereas the term induced current is applied, as previously stated, to what has been and is still often called the Faradic current. That term is now abandoned by engineers and in strictly scientific nomenclature. The difference in the characteristics of the various so-called "batteries" is marked, depending upon the character of the windings and arrangements between the primary and secondary. They vary from the small coarse wire coils used by our grandparents, and by some to-day, to the 20-inch Ruhmkorff coils now in use for producing the X-ray and high frequency currents. It is only the smaller apparatus, however, including the so-called high tension coils, that are considered under this classification for therapeutic purposes.

For *mechanical effects* they do not compare with the effects of the sinusoidal currents, and are not of practical use in the properly equipped office for that reason. The field open to this portable type of battery, in

which the source of electrical energy is a number of constant current cells, is for use at the bedside.

With the high tension coil, the contractions produced by a slowly interrupted current are often effective at the bedside for stimulating superficial metabolism, for relieving myalgia, and for application to the motor points for inducing muscular exercise by nerve stimulation. Some physicians, however, who are limited in their armamentarium to a wall plate combining a high tension coil with proper current control and meters, are able to accomplish much in the treatment of various conditions with the induced current by employing special electrodes, such as the bipolar induced current electrodes, producing with the slowly interrupted current pronounced localized contractions which are stimulating, and to a small degree produce local tissue drainage, or removal of infiltration. These currents are often used successfully in the treatment of pelvic conditions, and about the eye and other delicate parts where small currents are sufficiently effective. The mechanical effects of the induced current are similar in action to the static and sinusoidal current, but far less efficient.

The Constant Current Interrupted

The constant current, when interrupted by breaking the circuit or labile method—moving an electrode about—produces muscular responses or contraction from strong currents with both the making and breaking of the circuit. This current is, however, objectionable for purely mechanical effects, because of the active electrolysis which is not selective for good, and is often deleterious.

Application of Electrical Currents for Thermic Effects

Under ordinary conditions heat is produced by the passage of a current of sufficient amperage through a resisting medium. The passage of electrical currents through the human body produces heat in the tissues from two qualities of the current, i. e., amperage and frequency. Potential influencing the current in overcoming the resistance does often, to a degree, lessen its thermic effects.

For its thermic effects as a therapeutic agent the constant current from the ordinary galvanic cell, from the direct current of the commercial circuit, or transformer, produces an electrolytic action in the tissue which renders it objectionable except in cases where electrolysis or ionization may be indicated; neither is the *thermic effect* from a current strength that can be tolerated comparable with the same effect from the direct d'Arsonval current, on account of the superficial irritation produced by the constant current. Furthermore, the high frequency current is absolutely devoid of electrolytic action.

The high frequency current possesses the two qualities which influence the thermic action of the current—quantity and frequency—and can be employed with the greatest degree of toleration.

The hot wire meter used to measure high frequency currents is calibrated on the basis of the current strength of the constant current, that will cause equal expansion of the same wire which regulates the movement of the needle on the dial. It is a well recognized fact that, when a high frequency current passes through this same meter, the indicated milliamperage of the current is in excess of the actual current strength. This is due to the additional thermic action of the oscillatory current passing over the wire.

This disparity is best illustrated in the current derived from a static machine, which primarily generates a current not in excess of 1/4 to 1/2 of a milliampere, i. e., from a static machine having eight revolving plates. Such a machine, running at a rate of revolution of 500 or 600 per minute, may under favorable conditions produce a high frequency current which will register with the hot wire meter as much as 200 milliamperes. This apparent increase in current strength is due to two conditions: (1) the current flows into the Leyden jars, which are charged and discharged in such rapid succession that the current is always passing in a quantity equal to the capacity of the Leyden jars, and (2) to the frequency of the current, as previously stated.

The high frequency current for its thermic effect, particularly the direct d'Arsonval current, which is a current of relatively small voltage and large amperage, is, therefore, the current to be employed when electricity is indicated to be passed through the tissues for its thermic effects.

The *direct d'Arsonval current,* as shown in Fig. 6, passes the current between the two poles of the d'Arsonval circuit, directly through the tissues or part where the thermic effect of the current is sought. Various types of apparatus have been put upon the market during recent years for the purpose of producing a maximum thermic effect upon the tissues, i. e., to a maximum of tissue toleration.

For most effects the relatively high potential employed with resonators in connection with X-ray coils and transformers is adequate for producing these thermic effects. When, however, it is desirable to produce a maximum of thermic action, special apparatus designed to produce a high frequency current of low potential—2,000 to 8,000 volts—which may be administered in a current strength which will produce coagulation necrosis, when desirable, for the destruction of malignant tissue, neoplasms, or redundant growths. In this latter action the process effects much the same results as fulguration and desiccation. The technique will be given under the surgical uses of high frequency currents.

It should be borne in mind that, when the passage of a current of considerable strength through the tissues raises the temperature above

68° to 72° C., the tissues will undergo coagulation necrosis. It is desirable for this purpose to employ an arrangement for current production which will produce a thermic effect for both the induction of local hyperemia without local destruction of tissue, and greater temperatures when it is desirable to destroy superficial neoplasms. Care is to be exercised in the treatment of the deeper tissues with these strong currents. The sense of warmth or heat in the tissues, however, will be an indication in most cases against possible danger from an extreme action from the passage of the direct d'Arsonval current. When employed over ligamentous structures and scar tissue, care must be exercised against the danger of producing too extreme heat in the tissues, because they are meagerly supplied with blood-vessels and cannot be cooled, as other tissues are, by the flowing blood stream, nor are the nerves of sensation sufficient to give warning.

The relative size and position of the electrodes will determine with a fair degree of accuracy the location of the maximum of thermic action. If two electrodes of equal size are placed on opposing surfaces, the temperature will be found to be greatest at about midway between the two electrodes; whereas, if a large electrode be placed upon one surface and a much smaller one on the opposite surface, the field of greatest heat intensity will approach nearer the small electrode in proportion as the difference in size would average. In other words, when it is desirable to treat a condition in the skin, a large indifferent electrode may be used on one side of the body, and a small one on the spot to be treated. If a kidney or appendix is to be treated, place a large indifferent electrode on the abdomen or back opposite the affected part, and a much smaller one directly over the part. This arrangement of electrodes may be well estimated by considering the average of distance and difference in size of the electrodes.

The *physiological action* of the thermic effect of electrical currents upon the tissues is similar to that induced by heat from any source, i. e., the induction of hyperemia. As stated elsewhere, when a tissue is heated the blood supply is increased to that part through the influence of the vasomotor mechanism, in order to equalize or maintain the normal tissue temperature, the blood at normal temperature flowing in, to replace the heated blood which passes on, carrying the heat away by convection. The duration of hyperemia following the application will depend upon the excess of heat accumulated during the administration, and the additional varying period during which the vessels remain dilated. Taking advantage of this principle of vasomotor regulation, we are enabled to produce three effects in the tissues so heated by means of the hyperemia so induced: (1) The greater influx of blood with the consequent impulses upon the tissues exerted by the heart's force with the active passage sets up in the tissues a rhythmical transmitted pulsation which arouses greater

local tissue activity and metabolism. (2) The increased influx of blood carries with it increased nutrition to the tissues. (3) The increased blood supply carries also an increased number of phagocytes, thereby increasing the local tissue resistance or local phagocytosis.

Hyperemia produced by the direct d'Arsonval current is maintained during the passage of the current through the tissues, and persists for a considerable time after its discontinuance—until the tissues are cooled. When maintained for a considerable time with a current of relatively large milliamperage, the heating effect produced requires considerable time, often several hours, to dissipate the heat, particularly so in tissues that are not highly vascularized. The thermic action of the d'Arsonval current in inducing hyperemia for its effects on metabolism and nutrition is the current *par excellence* for producing these effects.

THERAPEUTIC INDICATIONS FOR THE THERMIC EFFECTS

The therapeutic indications for the employment of the d'Arsonval current in this manner are of great significance, as the effects produced would suggest, particularly in the treatment of infected tissues, where increased phagocytosis facilitates a destruction of the real cause of the inflammatory process—the germs present in the tissues. In all diseases in which the germs may be destroyed by the leukocytes or lymphocytes hyperemia induced in this way is particularly efficacious in relieving the tissues of the cause of the inflammation. *In the treatment of inflammatory conditions not due to infection,* in which, as previously stated, the static currents which produce tissue drainage are indicated, these currents, while to a degree beneficial, are not nearly so effective as the mechanical currents.

In the treatment of local infection, the interference with the activity of the phagocytes will depend upon the rigidity or stability of the wall of induration walling in the germ process. The heat acting upon the tissues exerts an effect of relaxation or tissue expansion, permitting a passage of the blood to a marked degree through the indurated wall. Otherwise it would be impossible, even with the hyperemia produced, to reach the germs which are causing the inflammatory process.

In low-grade inflammations of the tuberculous type the induration is never so marked as in the streptococcic or staphylococcic infections. *A persistent hyperemia* maintained under such conditions is peculiarly efficacious in effecting the destruction of the germs, when persisted in. This is practically demonstrated in the treatment of tuberculous glands by the persistent induction of hyperemia by the combined use of the direct d'Arsonval method with radiant light and heat. This is particularly efficacious in cases in which the process is not far advanced.

The method of applying the direct d'Arsonval current is by the application of two properly proportioned metal electrodes to the opposing surfaces, one on each side of an infected field, or when for other purposes the intervening tissue is to be treated. When, however, an infection is not at the surface on either side, or when an internal affection is nearer to one side than the other, as previously stated, it is customary to place a smaller electrode, about the size of the part, directly over the infected field, as of the involved tissues around an appendix, and an electrode of a size larger, relative to the distance between the part and the surface, where the smaller electrode is placed, on the opposing side, as over the back when treating appendicitis. A current is then employed which produces as much heat as can be easily tolerated beneath the smaller electrode. Ordinarily, through the body, a current of 1,000 to 1,500 milliamperes is well borne. In acute cases this treatment should be made twice daily, but ordinarily daily treatments will give good results in the treatment of infection. A great help to this method is the employment of the Roentgen ray for several days preceding the commencement of thermic applications, and the coincident employment of radiant light and heat with the direct d'Arsonval current.

THERAPEUTIC INDICATIONS FOR THE MECHANICAL EFFECTS

Treating the subject of therapeutics from the same point of view as of the physiological effects—*mechanical, thermic, and electrolytic*—of the electrical currents, will better convey to the student the indications for the employment of the respective modalities. To consider accurately the *indications for the mechanical effects of electricity* requires the recognition of a different point of view from the usual teaching or opinion relative both to the actions of electricity and the indications for its employment.

It is a generally conceived notion, even now dominant in the mind of the profession, that electricity is not indicated in the treatment of acute conditions, but in the subacute or chronic stage of an inflammatory process. When the writer first called attention to the error of this dogma in 1902, those observers who had given much study to the effects of electricity, the members of the American Electrotherapeutic Association, recognized and have since recognized the correctness of the views then expressed. The notion that electricity possesses some peculiar quality or action, which renders its employment dangerous in the treatment of acute disease, undoubtedly arose from the lack of a definite appreciation of the effect of currents which would mechanically disturb infection; for nothing could be more dangerous than the treatment of inflammation caused by infection by such currents. Mechanical currents break down

the induration which walls in a pus or other infectious process, thereby scattering the germs and rendering a local infection a general one. Too great objection could not be offered to the employment of electricity with mechanical methods in acute infectious inflammation. On the other hand, the high frequency currents which produce hyperemia without mechanical effects are employed, as previously shown, with great benefit in the treatment of infection, and the earlier the better.

The mechanical effect of electricity, particularly active when derived from the static machine, as shown in the paper referred to, is the most potent means of relieving one of the most prolific causes of chronic disease—localized induration, or stasis in inflammations of the non-infectious class.

Induration or stasis is an obstacle to restitution and repair, and not a normal process of the *vis medicatrix naturæ;* because a tissue through which the blood does not circulate, but is engorged, and which tends to persist in a swollen indurated condition, is a check to restitution and must be removed, either by exercise or some other external influence, which will soften the tissue and permit a return of the circulation. This principle in the treatment of inflammation has been long unrecognized, owing probably to the fact that there has been no known means of intelligently resolving it. It has been latterly recognized that, if a sprained ankle or other sprain is promptly strapped before swelling takes place, the recovery will be prompt. Massage has been invoked to dissipate the swelling of an inflamed part; but, except in the most skilled hands, and with the greatest patience, it is impossible to effect resolution without causing so much irritation that it promptly returns. For the same reason mechanical vibration applied directly to an inflamed tissue is a source of irritation, and of little consequence in the treatment of localized inflammation, except in its effects for the relaxation of muscular spasm remote from the site of the inflammatory process.

In the paper referred to the writer called attention to the significant fact that the local resolution of induration or stasis by the employment of the electrical modalities, which, by causing successive contraction of the tissues so indurated, expressed the infiltration and exudation through the lymph channels, and thereby drained the tissues without causing local irritation, removing the obstruction and pressure, and facilitating without irritation the restoration of circulation and repair. This is the fundamental principle upon which the mechanical effects of electricity in the treatment of inflammation are based. From this point of view, and with the proper modalities properly applied, it is possible to relieve the types of inflammation in which no germs are present when accessible; and there are few such conditions in which it is not possible to apply the current directly to the seat of the inflammation. The only sites in which difficulty arises are within the bony cavities of the chest,

immediately in front of the sacrum, and in the cranium. The neuromuscular mechanism of the trunk and limbs, the spinal cord, and pelvic organs are all amenable to this type of treatment.

ELECTROLYSIS AND INDICATIONS FOR ITS USE

Electrolysis is defined as the transformation of substances variously into their constituent parts by the passage of an electrical current through an electrolyte, of which they are a part. *An electrolyte* is a solution which conducts electrical currents, usually an alkaline solution, always associated with an electrolytic process when a current is passing. Solutions or substances which are not suitable as an electrolyte include pure water (H_2O), glycerin, oils, alcohol, paraffin, solutions of sugar, and numerous other substances. These, therefore, are not suitable electrolytes. When an electrical current is passing into an electrolyte, the acid radicals of oxygen basis in an electrolyte are set free around the positive pole, the anode, and move in the electrolyte, toward the cathode, and the metallic radical hydrogen is set free around the negative pole, the cathode, and passes toward the anode.

Ions, so named by Faraday (travelers), are the particles arising from the divisions which take place in the electrolyte and the substances of the electrodes; notably of the metallic electrodes at the anode, which are set free around the electrode by the action of an electrical current. At the positive pole, then, metals are broken up and diffused with the ions into the tissues, when employed in therapeutics in the form of metallic oxychlorides. This process is, therefore, called ionization. Metals employed at the anode undergo varying degrees of decomposition in point of rapidity and degree of diffusion, in the following order: silver, mercury, zinc, copper, and iron. Platinum is not diffused by the current.

Discoloration is produced at the positive pole in the corium when copper or iron electrodes are used for treatment of local skin conditions, copper producing a green stain which will be permanent, and iron a black one, contraindicating their employment in all cases at the positive pole for the treatment of superficial affections; whereas mercury, silver, and zinc ions produce no discoloration in the corium.

The oxychlorides of silver and zinc are diffused so rapidly that, except where destructive action is desirable, they must be used with caution. Copper electrodes amalgamated with mercury are best adapted to the treatment of internal conditions, including endometritis, hemorrhoids, and neoplasms in the mucous membrane. Mercury when used is employed as an amalgam over copper or zinc electrodes, as employed by Massey. Amalgamation is effected by dipping the electrode first into dilute sulphuric acid, and then into mercury, when the surface of the electrode will be evenly coated with metallic mercury.

For the treatment of angioma, facial epitheliomas, and conditions involving the skin, where destructive action is desirable, the zinc mercury electrodes of Massey, which produce no stain, may be used.

The *polar actions of electrical currents* are particularly important when employing the constant current for its important therapeutic effects; more so than their interpolar effects, because *thermic effects* for the induction of hyperemia for nutritional purposes are far superior when produced with the high frequency d'Arsonval current. While in the past, pending the developments of more recent methods of employing electricity, the constant current played an important rôle in therapeutics in numerous ways, it is no longer advocated to a large extent, except by the pioneers who may not have kept pace with these developments. The polar actions, as previously stated, produce oxychlorides of the metals at the positive pole with the effect known to be due to the affinity of oxygen, producing a drying or hardening effect of the tissue, with adhesions of the electrode to the surrounding tissues, unless the electrode is constantly moved during the administration. The accumulations there are distinctly acid, and the local action cauterant and destructive. To release a metallic electrode which has become adherent, the current should be turned off entirely by turning the current controller slowly back, and the polarity at the pole changer is next reversed. The current should then be turned on gradually, when the negative pole, then at the site where the positive has been, will soften the tissues, and the electrodes become loosened from the tissues. Great care should be taken to always carry out the details of these directions: (1) slowly turn off the current; (2) change the poles; (3) turn on the current gradually; (4) loosen the electrode slowly by gentle manipulation; (5) turn off the current, and (6) remove the electrode. Failure to carry out this order of routine will subject the patient to painful shocks and discomfort.

At the negative pole the hydrogen bubbles accumulate moisture in the tissues by decomposition of the electrolyte, which may be the tissues themselves, and, when so, it thereby destroys the life of the tissue, not properly as a cauterant, but by electrolysis. In this way it is possible to destroy *warts and scar tissue,* in a thoroughly practical and efficient manner. It matters not what metal is used as electrodes in these cases, iron or any other; for metals do not form combinations at the negative pole. The use of this pole as suggested is indicated for the removal of warts or other redundancies, as of scar tissue in the urethra, and for the destruction of hair follicles for depilation.

THERAPEUTIC APPLICATION OF ELECTRICITY

In pursuance of the plan outlined in the consideration of electricity from the three specific effects produced by electrical currents—thermic,

mechanical, and electrolytic—divisions or classifications of conditions to be treated are adopted in conformity with the types of diseases in which the respective activities of the modalities are indicated, irrespective of topical regions or other special arrangements.

Physical derangements or departures from the normal of health, called disease, are (1) in most cases associated, as to cause, condition, or effect, with an inflammatory process either with infection or without—infectious or simple inflammation—or (2) with a condition of altered metabolism which includes derangements of function, arising directly or indirectly from an inflammatory process, immediate or remote, or from inactivity, fatigue, toxemias, or other causes. Added to these are (3) the results of trauma, poisons, and malignant conditions (not to the present time determined to be of germ origin).

There are several therapeutic indications to be conserved when we look upon disease from this point of view: (1) The relief of infectious processes, and the resulting inflammation with a restoration to health, complete or incomplete from resulting conditions. (2) The treatment of simple or non-infected inflammation by the removal of local induration and restitution of local metabolism and repair. (3) The restoration to normal of impaired metabolism or local or general functional inactivities by awakening the systemic activities and restoring the normal relations of the nervous, circulatory, lymphatic, and muscular and digestive systems, which implies the restoration to activity of the functions of affected glands and special organs, with restoration also of normal tone, together with relaxation of muscular spasm, arterial, organic, and skeletal. (4) The destruction of malignant processes, keloid, condylomata, or other unnatural redundancies. (5) The correction of perverted mental or psychic manifestations arising from reflex or functional derangements or irregularities.

Special Therapeutics of Infections

Inflammation of infectious origin may be divided into two types: That which arises from direct local action on the germs in the infected tissue, and that arising from toxemia due to some remote infection. In both types the treatment should be first directed to the destruction of the germs wherever present. All germs that may be destroyed by the leukocytes or lymphocytes are removed by bringing the phagocytes into closer relation and in greater numbers into the field of infection. Where induration exists, surrounding the germs, circulation is coincidentally impaired, and, unless means are employed which will relax the induration and permit the flux of blood within, allowing the leukocytes and lymphocytes to come into proximity to the germs, the latter are certainly safe, and the process will continue. If hyperemia, however, is induced by

measures which increase heat, as applications of radiant light and heat and the direct d'Arsonval current, or superficially applications of high frequency currents with vacuum tubes, the tissues soften and relax, and the blood circulates where the germs are, and under conditions that are rendered particularly favorable to active phagocytosis, because the increased temperature is certain to inhibit the activity of the germs, and, when exposure to radiant light is added to the effects of heat, conditions are promoted favorable to positive chemotaxis. Heating the tissues, inducing as it does an active hyperemia, floods the parts with a stream of fresh arterial blood.

In early streptococcic or staphylococcic infection, before pus formation, the employment conjointly of means which resolve induration, as the static brush discharge, preceded by the application of radiant light and heat or the direct d'Arsonval current or the high frequency current from a vacuum tube, to the extent of inducing profound hyperemia, places the germs at the mercy of the phagocytes, and rapidly resolves the inflammatory process. This is well demonstrated in the treatment of suppurative tonsillitis, boils, carbuncles, and furuncles. If, however, the mechanical methods—those which induce tissue contraction—are used, after pus has formed, the results are apt to prove serious, as previously stated, because under these conditions the infection is likely to be scattered beyond all possibility of phagocytic control, and thereby set up an active localized or general infection.

In all cases of *local infection,* except those derived from the spirochetes or other germs, which are *not* destroyed by phagocytes, these methods are successful.

In all streptococcic, staphylococcic, tuberculous, and gonococcic infections, when the local conditions are under control, it is possible to effect successful destruction of the germ process, and restore the conditions to normal. When the process is already far advanced, however, the cure can be hastened, but not aborted.

The *X-ray* may be used in the treatment of infection to great advantage in conjunction with electricity, with the means which induce hyperemia and relaxation of tissue. In the treatment of localized infection its effects are due to its inhibitory action, which unfavorably affects all forms of germ life. When it is used it should be employed in pretty large doses a few hours preceding the application of radiant light and heat and the high frequency currents, all of which induce hyperemia.

Tuberculous Infections

In tuberculous infections it is customary, as in tuberculous adenitis and phthisis pulmonalis, to employ the Roentgen ray before the induction of hyperemia, with a view to inducing an inhibitory effect upon the tu-

bercle bacilli, or cause of mixed infection, or both. For the induction of hyperemia in these cases the conjoint employment of radiant light and heat, in order to produce its depressing effect upon the germs, should be followed by the direct d'Arsonval current with as much milliamperage as can be borne, for the purpose of inducing a profound tissue hyperemia, employing a degree of heat that will cause it to persist for hours after the treatment is discontinued, during which time the fresh blood stream will be flowing through the dilated vessels. This method usually proves effective in early cases, particularly in cases of adenitis and early joint tuberculosis. In other localized tuberculous processes, and in tuberculous peritonitis, the combined method with the X-ray offers more than surgical methods. These measures promise very much for the relief of local tuberculous conditions; and, in the writer's experience, the method has been successful in numerous cases.

Tuberculosis of the Skin.—In the treatment of tuberculosis of the skin—lupus vulgaris and lupus erythematosis—the method of Finsen not only produces a direct sterilizing effect from the ultra-violet rays upon the tissues, but at the same time induces a local increase of hyperemia designated by Finsen as the "reaction," which he considered important. Finsen's method with light is not nearly so prompt in these cases as the combined use of the X-ray and high frequency current, or static brush discharge, employing the former until there is a dermatitis, and then persisting in the recurrent induction of active hyperemia with the latter until the skin is normal.

Pulmonary Tuberculosis.—The value of the Roentgen ray in the treatment of tuberculous infections has been demonstrated by numerous observers, particularly so by Gibson of Denver, Colorado.

The writer, in a few cases which he had under observation, has substantially verified the position taken by this writer; but from the point of view that the germs—tuberculous and of mixed infection—are sterilized by the X-ray exposures.

The raying is usually carried to the point of producing dermatitis anteriorly or posteriorly, the irradiations being administered on alternate days, each time changing the side of exposure. After the appearance of the first dermatitis the X-ray is discontinued and the daily use of the direct d'Arsonval current and radiant light and heat is instituted, with a view to inducing active thermic effects in the tissues for the induction of increased hyperemia, thereby increasing locally phagocytosis and resistance of the tissues. The direct d'Arsonval current is applied with two large electrodes covering the pulmonary area front and back. The electrodes should be made of sheet metal, with the edges of the metal turned up, and then made to fit closely to every part of the surface. This method of turning up the edges of the metal electrodes is employed in all cases

where the d'Arsonval current is used for its thermic effect; because, unless the margins are rounded or very smooth, the current will discharge from points or sharp edges, and create a burning of the skin at the margins. Nagelschmidt places beneath the electrode a piece of thoroughly moistened cloth or absorbent cotton, which will offer no resistance to the current, and will conform evenly to the surface. It is necessary that the electrode should touch every part of the underlying skin, otherwise a sparking will take place where it is not in contact, producing a burning sensation, which may require frequent removal and readjustment until there is no sensation whatever except the warmth produced by the passing current. When properly applied very little hyperemia is produced in the skin by this method, but in the tissues beneath. It is needless to say that the regulation of diet to the requirements of the individual (not by forced feeding) is indicated in these cases. Furthermore, that, where hypertension is present, it should also be regulated by methods described elsewhere.

Tuberculous Adenitis.—Tuberculous adenitis has been treated with marked success by the Roentgen ray for upward of ten years, until that method has become generally recognized as a practical method of curing this condition. The method usually employed is to make successive series of rayings until every evidence of activity in the process has disappeared. That method is fraught with an unfavorable action upon the skin if several series of exposures are necessary, often ending in a disfiguring telangiectasis. This has led the writer to adopt the following plan of treatment: In the earliest stages daily application of radiant light and heat, followed by the direct d'Arsonval method, placing an electrode about the size of the gland or glands directly over the swelling, and one on the opposite side of the neck of much larger size, produces in the gland a degree of hyperemia which will, in most cases, successfully clear out the germs present, and effect a complete cure.

In *advanced cases* of adenitis, before mixed infection with suppuration has intervened, the employment of one series of X-ray exposures, i. e., until a dermatitis is produced, and then followed with energetic applications of radiant light and heat and the direct d'Arsonval current, placing the electrodes as previously stated, is successful in most cases without further exposure to the X-ray. This method should be employed daily in order that the hyperemia may be nearly persistent, thereby effecting a complete destruction of the tuberculous germs causing the condition. Under this plan of treatment the general health of the patient will rapidly improve, indicating a cessation of the infection. When it is certain that the germs are destroyed, the resulting infiltration or thickening of the gland can be largely dissipated by employing the static wave current or the vacuum tube current, with a suitable electrode applied directly over the gland. Care must be exercised that in this last

procedure it is not instituted before the germs have been destroyed, lest the infection be scattered.

By this combined method neither the skin nor the functions of the gland are impaired if treated early. It is needless to add that in all these cases the tonsils, which are the usual source of infection, should be properly treated; for which the electrical method of fulguration, described elsewhere, is effective.

Tuberculous Prostatitis.—Tuberculous prostatitis may be diagnosed or suspected when treating the prostate by the usual method described elsewhere, if the condition is aggravated, i. e., the vesical irritation and prostatic symptoms are made worse by the treatment. If the condition is aggravated by the wave current, it will indicate that there is either a tuberculous or malignant process, or that there are calculi in the prostate.

The writer has successfully treated these cases by employing the X-ray through a metal screen having an opening three or four inches in diameter placed directly over and below the coccyx, directing the rays upward. The exposures are continued until a dermatitis appears, when the raying is discontinued. Radiant light and heat and the direct d'Arsonval method are then applied for their thermic and hyperemic effect. With the latter either place a metal or vacuum electrode in the rectum directly in contact with the gland, and a large indifferent electrode over the abdomen. As many milliamperes as can be comfortably tolerated by the patient should be employed, the sensation being one of heat at the side of the rectal electrode. By this method it is possible to induce active hyperemia in the gland, which will produce no aggravation but relief of the symptoms, and ultimately terminate the infectious process.

Tuberculosis of the Bladder.—In tuberculosis of the bladder the method would be varied from the preceding by raying above the pubis, and then following with radiant light and heat and the direct d'Arsonval current anteriorly, by placing a small electrode about three or four inches in size directly above the pubis and a large indifferent electrode upon the back of the patient. With these large electrodes the milliamperage, as measured by the hot wire meter, should be from 1,000 to 1,500 milliamperes, or more or less, as the patient tolerates the current, and the applications should be administered daily, or twice daily when possible, as in all cases when hyperemia is to be maintained in accordance with the principles of the method.

Tuberculosis of the Kidney.—Tuberculosis of the kidney may be treated on the same general principle as the two preceding conditions. After the usual X-ray series, radiant light and heat and the direct d'Arsonval method should be employed. It is possible by catheterizing the ureter to discover which kidney is involved, the urine having given evidence of the lesion in that region. In this case it would be only necessary to make the applications to one kidney; otherwise it would be necessary to treat both kidneys in the same way. As hyperemia can do no injury to the

unaffected kidney, there will be no contraindication against applying the current to both. In this event, however, the indifferent electrode should be placed over one-half of the abdomen, and one about the size of the kidney directly over one kidney, and then repeat the treatment, removing both electrodes to the opposite side, thereby preventing overstimulation of the intervening tissue. This method may also be employed in the treatment of other kidney lesions, including pyelonephritis and parenchymatous nephritis, according to the method of Dr. Nagelschmidt of Berlin.

Tuberculous Peritonitis.—Tuberculous peritonitis, treated by the mixed treatment above described, promises most brilliant results. The Roentgen ray has been successful in numerous of these cases when employed alone. Gibson of Denver has reported numerous successes by this method. The combined employment, however, of radiant light and heat and the direct d'Arsonval method by the thermic induction of hyperemia, following a series of X-ray exposures, offers the added benefit indicated.

Tuberculous Arthritis.—Tuberculous arthritis, treated by the mixed treatment, X-ray, radiant light and heat, and direct d'Arsonvalization, is remarkably successful in early cases, before the bone is involved or structural changes have taken place in the ligaments or synovial membrane. To derive the best results, however, from this plan of treatment, the direct d'Arsonval and radiant light and heat should be used, when possible, twice daily. The direct d'Arsonval current should be used for at least twelve minutes, and with a current strength regulated to the toleration of the patient at each administration, placing the electrodes upon the opposite sides of the knee joint. Another method, when it is desirable to produce a general hyperemia in the joint, is to place a metal electrode immediately above the patella, and another one over the gastrocnemius just below the popliteal space, and pass a current of 1,000 to 1,500 milliamperes, or more if tolerated, through the tissues. This method was recently described by Dr. Nagelschmidt of Berlin, but has not appeared in any contribution by him.

Pyogenic Infection

The treatment of pyogenic infection by electricity should follow very much the same routine as in the treatment of tuberculous infection, the principle being practically the same, though in streptococcic infections it is not good practice to prolong the period of raying, as in tuberculous infections, except in indurated acne, but to employ one massive dose. In ten or twelve hours the raying should be followed with an energetic administration of radiant light and heat or the direct d'Arsonval current, one or both, as the conditions indicate. The rapidity of the progress of these infections, and the seriousness of delay, will not permit the pro-

longed course of treatment prescribed in the treatment of the more subacute conditions.

Carbuncles.—Carbuncles in the first stages are diagnosed by the extent of the area of tenderness with induration, with possible indications of one or more sinuses with slight vesication at the surface, indicating the presence of an extensive area of infection. When cases come under observation before suppuration has intervened, the application of the X-ray should be made for fully thirty minutes with an intensity approximately indicated by one milliampere of current passing into a low vacuum tube supported at a distance of twelve to fourteen inches from the patient. There is absolutely no danger from this long exposure in any case, and it is important in order to produce a profound effect upon the germs present. In twelve hours this exposure should be followed by a very long application of radiant light and heat, as intense as can be tolerated. This will offset any deleterious effect that might have occurred from the ray, besides inducing an active hyperemia. Follow this immediately by the application of the direct d'Arsonvalization method with a metal electrode placed directly upon the skin, or with an intervening wet material, as gauze or absorbent cotton, the edges of the electrode having been turned up, and even pressure being distributed over the surface. On the opposite side of the body a large indifferent electrode is placed, and this current is continued for twelve to fifteen minutes, or even for a longer time, regulating the current strength to the toleration of the patient, and employing approximately 1,000 to 1,500 milliamperes of the current, or more if tolerated. In severe cases radiant light and heat and the high frequency current should be employed twice daily. In two or three days the lesion will, in most cases, have absolutely disappeared, and the carbuncle will be aborted. The method of treating this severe type of local infection best illustrates the general routine for relieving other cases of infection with electricity.

Boils and Whitlows.—Boils and whitlows will be treated in practically the same manner, unless in the very early stages, before any pus has formed, an application of the direct d'Arsonval current for the induction of intense hyperemia, either employing a metal electrode about one inch in diameter, or for the active electrode employing a vacuum electrode until the skin is very hyperemic over an area two or three inches in diameter; after which apply the static brush discharge until the indurated area is softened. The active hyperemia thus induced will often facilitate the prompt destruction of the germs and arrestment of the process.

A *felon or whitlow* will be cured very promptly in the first days by placing the painful surface of the finger in the depression of a vaginal electrode and employing the wave current method, regulating the spark-gap to the toleration of the patient. It must hurt considerably to dis-

sipate the induration. The current should be continued until all pain, except that of muscular contraction or cramp, has disappeared, when the induration will have disappeared from the finger. Two treatments in this manner will abort a felon on the first or second day without danger of setting up a diffuse infection. The same thing can be accomplished with the static brush discharge applied until the induration is dispersed. It is advisable here, as in the treatment of boils, to employ radiant light or the high frequency current from a vacuum tube, until the finger is thoroughly hyperemic, before employing the mechanical method described.

Furuncles.—Furuncles may be treated by the same methods as the lesions described, care always being taken not to use a mechanical method where pus is present.

Suppurative Tonsillitis.—Suppurative tonsillitis may be treated on the same principle exactly as boils and whitlows. On the first days, before the temperature indicates the presence of pus, the induction of local hyperemia by either light or the direct d'Arsonval current, or both, followed by the static brush discharge, wave current, or direct vacuum tube current, applied externally over the indurated area, will dissipate the induration and cure the condition. The writer has obtained this result so often in these cases that he cordially advises the employment of the method.

Otitis Media, Mastoiditis, and Suppuration of the Frontal Sinuses and Antrum.—See chapter on Light Therapy.

Appendicitis.—For *acute* appenditis see chapter on Light Therapy.

Chronic appendicitis may be treated in very much the same manner as tuberculous infections, using the X-ray for a series of exposures for the purpose of destroying any local infection present. This is to be followed by the direct d'Arsonval method applied practically the same as for the treatment of tuberculosis of the kidney. The results in these cases are very satisfactory, unless the appendix has become adherent to the intestine, ovary, liver, or abdominal wall. The treatments, however, may have to be continued for a month, and rarely longer, before the tenderness is entirely dissipated.

Abscess of the Colon, Mesentery and Liver.—The same principle of treatment is to be employed here as in external abscess. In the descending colon, however, it is often possible, after the ray and direct d'Arsonval have been employed, to use the static wave current with safety to remove the infiltration, the infection having been destroyed by the light and direct d'Arsonval following the Roentgen ray.

Pyelonephritis.—Pyelonephritis may be treated in practically the same way as tuberculosis of the kidney, and with a fair prospect of success. One case, however, in a child has been reported by Dr. West of Philadelphia, in which the wave current was employed over the kidney, and

which resulted in a complete evacuation of the contents through the ureter, followed by complete recovery.

Infection of the Extremities.—Localized extensive infection of the extremities is most successfully treated by the induction of hyperemia with dry heat by means of the local dry hot-air apparatus. The direct d'Arsonval method, however, is practicable when the infection is localized; but, when extending the length of the limb, it is not so effective and certain as the treatment by dry, hot air, which induces active hyperemia in the whole length of the limb. (See chapter on Light Therapy.)

Pelvic Cellulitis.—Pelvic cellulitis should be treated on the same general principles as other septic processes. A cylindrical metal electrode, as large as can be conveniently placed in the rectum, should be placed as close as possible to the area of local tenderness, and a large abdominal electrode be placed directly opposite above the pubis. A current of 800 to 1,500 milliamperes, according to the toleration of the patient, should then be passed for from ten to fifteen minutes. This administration should be preceded or followed by a prolonged exposure to radiant light and heat.

Indurated Acne.—When the pustules are very numerous, the most successful method of treating this trouble is with the Roentgen ray, always carrying the exposures to the induction of dermatitis, and following the irradiation with the employment of high frequency applications from vacuum tubes.

When the nodules are discrete and scattered they may be cured before advanced to suppuration by inducing (1) a very active hyperemia with the high frequency vacuum tube, and (2) applying the static brush discharge or the vacuum tube wave current until the induration is removed. By this method the phagocytes are capable of destroying the infection. When this method is adopted it is prudent to make applications of the glass vacuum tubes to the extent of producing extensive hyperemia over considerable surface surrounding the pustules, in order that the diffused hyperemia may, by increasing the local presence of the phagocytes, clear up the tissues from any bacteria present, and at the same time produce a more active metabolism in the skin.

Gonorrheal Infections

In acute gonorrheal infection it cannot be shown, except in the very earliest stage, that the usual electrical methods of treating infections are especially effective. It is probable, however, that a technique will be developed which will succeed in arresting the process at any stage. In the chronic conditions, however, the results are eminently successful, and deserving of very thoughtful consideration by those who have not yet given attention to these subjects.

Vesiculitis.—Specific vesiculitis, than which probably there is no more vicious scourge, especially in its effects on the female, is treated with fairly uniform success by the employment of direct d'Arsonvalization, using a rectal vacuum electrode, the insulated tube of Dr. Titus allowing a greater degree of concentration, because the current is diffused otherwise the whole length of the tube. The local heat produced, however, will be relative to the surface, and, therefore, with an abundant milliamperage of current, it is possible to use the uninsulated tube with equal success.

A misconception exists in the minds of many, and with some writers, we regret to say, with reference to the dispersion of the current from a tube placed in the rectum or other cavities. It has been said that, unless the tube is insulated, the current will all be given off at the entrance to the anus. The fallacy of this opinion can be readily demonstrated by holding a vacuum tube in the closed hand, and, with the fingers separated, noting that the discharge goes equally to each finger in contact, or to one placed on the extreme end of the tube.

The static wave current should be applied in the treatment of gonorrheal vesiculitis, following the application of the high frequency current, with a view to evacuating the contents of the gland. If this treatment is administered daily, it is remarkable how soon the shreds and other evidences of infection disappear, and, when continued for a month or six weeks, it is in most cases impossible to find by any means evidences of infection. The prostate gland is treated coincidently with the treatment of the vesicles, thereby treating the whole of the upper genital tract for removal of the infection.

Gonorrheal Prostatitis.—Gonorrheal prostatitis is treated by practically the same method as the uninfected cases of prostatitis (see Prostatitis).

Epididymitis.—Epididymitis is promptly cured by the application of the vacuum tube wave current with a suitable electrode, or the wave current with a metal electrode formed to fit the parts directly over the epididymis. Most of the pain and tenderness will disappear at the first treatment, if thorough; a few succeeding treatments completing the cure. While this may seem incredible to those unfamiliar with the method, the effect is explained purely by the mechanical action of the current, it removing the induration and infiltration present in the tissues. Following the application of the mechanical treatment, after the tissues are stimulated by the exercise, there will always be an increased flow of blood for a time through the parts. It is during this hyperemia that the phagocytes remove the cocci present.

Salpingitis.—Salpingitis is treated under practically the same principles as the other infections, by placing a vaginal electrode in position against the cervix and a metal electrode above the pubis, and employing

the direct d'Arsonval current. The results in these cases are uniformly good in early cases.

Pyosalpinx.—Pyosalpinx may be treated by the employment of the direct d'Arsonval current with a metal or glass electrode placed high up in the rectum, and a large abdominal plate placed above the pubis, using a fairly large amperage of current, 1,000 to 1,500 milliamperes for ten or twelve minutes daily. The results from this method in the early stages of pyosalpinx are very effective, and there is no danger whatever from the administration, and a prospect of success in many cases. Another method which is more heroic, and not free from danger, but which has proved effective in cases in other hands, is by the use of the direct vacuum tube current. A vaginal electrode is placed against the cervix with the patient lying upon her back on the static chair, which is placed upon the insulated platform; the spark-gap is then gradually lengthened to three or four inches, and treatment continued for twenty minutes. By this method the contents of the tubes are forced out and evacuated through the uterus, owing to successive contraction and release induced throughout the uterus and appendages, and the condition relieved.

Diseases of Toxic Origin

Under this classification are numerous conditions which have often been designated as "rheumatic" instead of toxic infections, under the delusion of what was long designated the "uric acid diathesis." They include the various types of arthritis, and various heart and throat lesions, which have their origin usually in derangements of the intestinal tract, arising from defective metabolism associated with impaired digestion, secretion, and absorption.

The part played by electricity in the treatment of these conditions may be divided into three distinct effects: (1) The restoration of tone, metabolism, and increased activity, with a disposition to evacuations by the employment of the mechanical currents—the static wave current, or sinusoidal current. (2) The thermic currents as applied increase hyperemia, effecting also an increase in nutrition and metabolism of the abdominal viscera, and (3) an increased energy of the system in throwing off excesses of various intestinal flora, with evacuation, thereby preventing the possibility of decomposition of the feces. When constipation is present, other means are often necessary for a time in connection with mechanical currents to effect the removal of the intestinal contents. In order that the pabulum upon which the bacteria can develop be limited, the food consumption should be carefully adapted to physical requirements, and not in excess. Primarily the treatment of toxic infection must look to the removal of the causes as here suggested.

Joint Inflammations.—The local treatment of joint inflammations, as

rheumatoid arthritis, gout, and other arthroses of intestinal origin, consists in the employment of means which restrict the growth of germs and institute more active metabolism in the structures of the joint by the removal of infiltration and the establishment of active circulation in the tissues. This may often be accomplished best by the administration of the static wave current, applied by placing metal electrodes securely over and around the joints where the current will produce most effect, avoiding bony prominences. The electrodes may be cut in various shapes adaptable and molded about the joint.

The *direct d'Arsonval current* may also be used often to advantage in these cases by applying electrodes on each side of the joint, and passing the current directly through the synovial membrane of the joint, thereby increasing the circulation and metabolism and promoting the elimination of the toxic poisons, which may have aggravated or caused the active inflammatory condition in the joint. This method is applied as previously described in the treatment of tuberculous arthritis.

Gonorrheal Arthritis.—Gonorrheal arthritis is cured with the greatest promptness in most cases by the treatment of a local gonorrheal vesiculitis and prostatitis, which are the usual source of the toxemia. The pain and active process usually disappear within three or four days after daily treatments are instituted, except in the very chronic cases, when it may require the additional employment of static sparks, and the direct d'Arsonval current directed to the affected joints.

Pericarditis and Endocarditis.—In pericarditis and endocarditis, with the usual attention paid to the alimentary canal and diet, the local treatment should consist of prolonged and frequent local applications of radiant light and heat, and the direct d'Arsonval method, with the current applied directly through the cardia with the usual technique employed with reference to dosage and position and size of electrodes in the treatment of other viscera.

Pharyngitis and Laryngitis.—In toxic pharyngitis and laryngitis the usual routine of dietary régime, together with the local use of radiant light and heat and direct d'Arsonvalization, with systematic inhalation of antiseptic substances, usually promptly relieves the local congestion and irritation present in these cases.

Simple Inflammation

The designation of simple inflammation signifies an inflammatory process which, though infection may be primarily the origin, is not characterized by the presence of germs at the site of the active inflammation.

The *origin* of inflammation of this type may be (1) from mechanical or chemical injury, (2) defective metabolism, or (3) toxic causes.

The *conditions presenting in local inflammation* of this type are char-

acterized at the onset by (1) an increased vascular dilatation with rapid influx of blood, which directly engorges the tissues, resulting in (2) swelling, induration, or stasis. (3) Pain under these conditions may be absent except when pressure is applied to the indurated tissue, or the induration may be so pronounced that pain is constantly present, due to marked pressure upon the end nerve filaments. (4) Round cell infiltration and extravasation of fibrin and other products of inflammation promptly fill the intercellular spaces, and the tissues become more hardened and sensitive to pressure. (5) Organization takes place if inflammation once present and unresolved becomes chronic with the organization of hyperplastic or scar tissue—poorly nourished tissue of low vitality. This is the usual clinical picture of localized inflammation, resulting from an accident over which nature has but moderate control; and when "left to nature," as has been the oft-repeated saying, results in chronic inflammation and disease. As a consequence, the tissues (1) become hypertrophied and deformed, (2) with a tendency to the formation of plastic adhesions, with ankylosis of movable parts; (3) metabolism is absent or impaired in the parts affected; (4) resulting in derangements of function, and in some cases degeneration and destructive processes are instituted under these conditions.

The *treatment* of inflammation must soon be recognized as properly the field of *electrotherapeutics*. The general recognition of the principles involved in the treatment of these conditions will lead to the early relief of a very large part of human suffering.

Treatment of a sprained joint will well illustrate the principles involved in the treatment by electricity of inflammation which is not infected. It was the treatment of such a case that first led the writer to discover the method and principle of employing mechanical currents for the treatment of inflammation. The present, generally accepted, method of treating a local contusion or sprain is the early application of adhesive straps firmly applied to prevent the engorgement of the tissues, following the injury. It is a well-established fact that under these conditions the sprain more rapidly recovers than by the older method of rest and elevation. By this method, however, it is impossible to entirely prevent infiltration of the tissues, because it is not possible to prevent the collection of blood in the synovial membrane, and over spots where it is not possible to make firm pressure. If massage, manipulation, or the application of mechanical vibration is applied, except with the greatest gentleness, and then only in selected cases, it may be possible to dissipate the infiltration; but any measure which, when applied, produces a degree of irritation will be promptly followed by a recurrence of the swelling.

Theoretically, and practically, two methods are successful in affording relief in the very earliest stage of involvement: (1) one which pro-

duces a very intense hyperemia, with dilatation of the capillaries, may permit the blood to flow on through the injured part and thereby not obstruct or engorge the tissues. Measures which may succeed are the prompt application of radiant light and heat, or the direct d'Arsonval current, or both. (2) The application of mechanical electrical currents, as the *static wave current,* when applied to the site of an injury, produces successive contraction and relaxation, and thereby propels the blood stream on through the tissues, and prevents swelling or an accumulation of infiltration. The latter is certain to be the most effective measure.

When *swelling and induration* are once established, however, the method by induction of hyperemia will not again open the channels of circulation and relieve the local swelling. It is in such cases, therefore, that the high frequency currents and radiant light and heat fail in the treatment of inflammation, and it is in these same cases that the static modalities occupy the field unrivaled in the treatment of the type of inflammation under consideration. The *static wave current,* the *static brush discharge,* and the *static spark,* alone or in combination, as indicated, are capable of dissipating infiltration or local stasis. If persisted in most of the induration and infiltration following a severe injury of the joint will be removed. This will permit a disabled patient to use the part with very little pain or suffering after the first treatment. Though this operation may require from thirty minutes to an hour, the result is positive, and the condition is practically cured at the first treatment, though two or three succeeding applications of a similar sort will hasten a complete restoration of a part. It is only in conditions in which a bone or ligament has been ruptured that these results are not obtained in early cases by the following method:

The *usual routine* is to apply the static wave current with electrodes fitted gently over and in close contact with the affected part, for twenty minutes. This should be followed by a thorough application of the static brush discharge over the whole of the swollen area, until the tissues are well softened, and then static sparks should be applied, localized with a spark director into the hollow spaces and interstices between the bones of the joint. After this the joint will be moved with little or no pain. The novice may attempt this operation by a negligent method and fail, as will the prejudiced operator who is not willing to believe it possible to obtain these results.

The *scope of indication* for the employment of this mechanical method of relieving the tissues from induration and infiltration is very wide. From the application of a small vacuum electrode over an obstructed tear duct, to the treatment of the inflamed tissue of a sacroiliac joint, and including congested and infiltrated viscera not the seat of an infected or malignant process, is the scope of employment of the mechanical currents in the treatment of inflammation. These methods have only to be

investigated to be recognized, when they must be accepted by the profession at large. Specifically considered, the scope of this method includes the treatment of a very large number of local conditions.

Associated with inflammatory conditions, reflex muscular spasms are always present near the seat of inflammation. As these conditions are likewise removed by the mechanical effects of the current, they will be referred to in connection with the treatment of each inflammatory affection. There is no measure in therapeutics so active and energetic in relieving muscular spasm of the skeletal muscles as the static currents applied directly to the muscle, either in the form of the wave current or the static sparks. A few applications of static sparks are remarkably effective in relaxing muscles in a recent state of spasm, as present with neuritis and the early stage of joint inflammation. Joint fixation by muscular spasm has unfortunately been looked upon as indicating part of "nature's method" of curing joint disease. In other words, it has been frequently said by orthopedists that because nature puts a part to rest it should guide us in our action in the treatment of these conditions. Nothing is more fallacious than such an assumption. As well say that stasis is a part of the plan of the *vis medicatrix naturæ* and not an accident, for both are direct obstacles to improvement and recovery, the one interfering with the motility of a joint which would assist in removing the stasis, and the other preventing repair by arresting local metabolism at the site of the injury. No greater error can exist than the assumption that inflamed parts, except fractured ones, should be put at rest. This has too often resulted in joint ankylosis, which *is* "nature's method" of cure. In chronic neuritis rest has often been employed for the treatment of sciatica, when the rational method with the relief of inflammation and muscular spasm will permit movement and hasten recovery.

Three essential rules are to be observed in the treatment of every non-infected inflammatory process: (1) the removal of local induration or stasis; (2) the institution of systematic exercise, moderate at first, and gradually increasing; and (3) the relaxation of muscular spasm in the vicinity of the lesion. With these premises the treatment of non-infected inflammation resolves itself into a very simple proposition, which is essentially the field of electrotherapeutics; for no other agency or measure is so effective in relieving local inflammation of this type as the currents which produce the mechanical effects described.

Inflammation of Joints

The treatment of a sprained joint has been thoroughly outlined in the premises; and the method constitutes practically that employed in the treatment of every type of joint inflammation, except the fractured and infected cases.

Synovitis.—In synovitis, acute or chronic, with the absence of an infectious element, and when the parts are otherwise normal, the prognosis is uniformly good. They will be cured in most cases in a time relative to the chronicity of the condition. Acute joint inflammations of traumatic origin are cured in a few days; whereas conditions which have been present for several weeks or months will require weeks or months to effect a complete restitution, and in some cases, after two years, changes may have taken place in the joints in the form of villous hypertrophies, and other defects which may to a degree leave the joint impaired, and in which surgical intervention under modern skilled methods may be required to effect a complete cure. In a very large percentage of cases, however, no such intervention will be required. In many cases the improvement will be further hastened by the administration of the direct d'Arsonval current through the joint, following the wave current and sparks or alternating with the static treatment; the object of the former being to remove induration and infiltration, and the latter to increase metabolism and nutrition by increasing hyperemia.

In addition to the treatment of the local inflammation the operator should always apply either the sparks or the static wave current to contracted muscles, until each muscle is relaxed. This relieves the pressure between the joint surface, removing an element which interferes with nutrition. In cases of rheumatoid arthritis and spondylitis deformans this pressure hastens the destruction and absorption of the interarticular cartilages. It will be noted that, in cases of spondylitis deformans, the skeletal muscles are largely in a state of tension, including the rectus and other abdominal muscles. No treatment affords so great relief from the suffering of these unfortunates as the relaxation of all muscular tension.

Sacroiliac Disease.—In sacroiliac disease an important diagnostic point is the presence of tension in the glutei, the adductor magnus, and the psoas muscles, and no part of the treatment of this condition assists more in its cure than the relief of the tension of these muscles. This is accomplished by the application of the static wave current with a flat metal electrode 4 or 5 by 12 inches, applied over the glutei muscles, extending up over the lower end of the quadratus lumborum. In ten or twelve minutes, by employing a gradually increased length of spark-gap, a complete relaxation of these muscles is effected. The application subsequently of another electrode over the adductor magnus will also relax the tension of that muscle. The presence of pain in the muscles when the wave current is administered is diagnostic of muscular spasm, and suggests the presence of sacroiliac disease. The current should be administered daily or twice daily, in acute cases of sacroiliac luxation. In addition the patient should be instructed morning and evening to exercise, raising and lowering the abdomen, supporting the weight upon the heels

and shoulders. This is done to overcome the tension of the psoas muscle, and to assist in bringing the bones into normal position. By this combined method the acute luxation of the sacroiliac in the first days may be promptly cured within a week or ten days. In the more chronic cases a longer time will be required, and the prognosis will be bad in all cases after eighteen months or two years of displacement.

Rheumatoid Arthritis.—In rheumatoid arthritis, where so many joints are affected, the larger joints or the ones most seriously involved may be treated with the wave current or direct d'Arsonval, or both; and all of the smaller joints and contracted muscles should be sparked until the parts are thoroughly relaxed. This, together with the employment of light baths, and, what the author has found of supreme importance for the purpose of removing the ever-present intestinal putrefaction—the daily administration of high colonic flushings and the institution of a rigid non-putrefactive (vegetable) diet. There are few of these cases in the early stages that cannot be cured by proper dietetic and electrotherapeutic régime.

Tenosynovitis.—Tenosynovitis in the early stages is very promptly relieved and cured by the application of the static brush discharge, wave current, and sparks to the extent of removing the local infiltration. The crepitus readily disappears, and, in cases even of several weeks' standing, the cure is often effected in a few days. In some cases the additional employment of radiant light and heat and the direct d'Arsonval current will hasten the restitution, and there is no objection to their use in all cases.

Neuritis

Neuritis should be treated from the point of view of a local inflammatory process, the same as any other local inflammation. Usually in the early stages the inflammation involves the perineural sheath, and in some cases the surrounding structures as well. Only those cases should be designated as neuralgia in which the pain is due to pressure without inflammatory involvement of the structures of the nerve itself. Clinicians too frequently consider the seat of pain as the site of the lesion, which is a serious mistake from the therapeutic point of view, because the local lesion requires treatment to relieve the pain. It should be borne in mind that pain indicates a lesion or pressure upon a nerve somewhere in its course or in the neurons, and is referred to the periphery.

The *diagnosis* or *localization* of a neuritic lesion is, in most cases, accomplished with great facility.

The author's method, which he first described in his work on "Static Electricity and the Uses of the X-Ray," is to place a small electrode over the suspected site of the lesion, when, if great pain is produced by a short spark-gap, when

the wave-current is applied, the suspicion is confirmed. Otherwise it will be necessary to place the electrode at some other place where the lesion is most apt to be. The inflammatory affection in neuritis is as a rule circumscribed within a small area. The fact that these localized areas have not often enough been recognized has led to the abuse of the term neuralgia. As stated in a former article by the writer, there are certain exposed regions which are common sites of neuritis. Such lesions are usually located at points where the nerve trunk crosses a bony prominence or fibrous structure, particularly when a muscle is over a nerve in an exposed part of the body, as in the following frequent sites of neuritis: where the sciatic nerve at the sacrosciatic notch passes beneath the pyriformis muscle; where the crural nerve passes beneath Poupart's ligament; where the lumbosacral cord and the anterior crural cross the sacroiliac synchondrosis; where the musculospiral and circumflex emerge from beneath the teres minor; where the suprascapular passes out beneath the trapezius and enters the supraspinatous fossa of the scapula; where the inferior-dental enters the canal in the inferior-maxillary bone; where the superior-maxillary or second division of the fifth cranial nerve emerges through the infraorbital foramen. These exposed points and many others explain the traumatic origin of a large percentage of the cases of neuritis, the peculiar conditions accounting for frequent occurrence at these sites.

In *herpes zoster* and *intercostal neuritis* deep pressure made in the intervertebral spaces over the posterior roots will often elicit points of tenderness.

The *treatment* of neuritis should be directed to the relief of the local inflammatory condition. In cases of toxic origin there will be relief from the employment of intestinal evacuation and antiseptics. Rest and local applications of light and heat are of little avail if the lesion is considerable, or comes late under observation.

The *writer's method of treating neuritis,* which he has employed in more than nine hundred cases, has met with uniform success when the lesions have been accessible. The method is in accord with the general principles of the treatment of inflammation with the static modalities. The application of the static wave current is made over the lesion, and static sparks and the wave current are employed to overcome the complicating muscular tension.

The general plan is to place a metal electrode of soft pliable metal (22 gauge) over a site considerably larger than the lesion, in such a manner that the metal is held usually with a pillow in close contact with the skin. The static machine is started at a slow rate of speed, and the spark-gap gradually opened as the toleration of the patient will permit, always insisting that the patient bear a moderate amount of pain. Otherwise very little relief can be afforded from the treatment, because the contraction of tissues induced over an inflamed area increases the pressure and pain. As the pain with a given spark-gap diminishes, the gap should be gradually lengthened during the full twenty minutes. At the first treatment there will be pain during the full period of treatment. While this is depressing to the patient at the time, the relief afforded is so great that patients rarely complain at the second treatment.

In severe cases of acute neuritis the applications should be made twice daily, and, as the condition improves, daily treatments are to be continued until the condition is practically cured. The results from this plan of treatment are always effective, if the technique is properly carried out, and the lesion is accessible. Neuritis in different parts requires some special electrode and technique for treatment.

Sciatica.—When the lesion is at the notch begin with a spark-gap usually of not more than three-quarters of an inch to one inch, sufficient to cause an endurable local pain, and then lengthen the spark-gap gradually as the pain becomes less for twenty minutes, at the end of which time the spark-gap may be lengthened to approximately three or four inches, varying with conditions. At each succeeding treatment it should be possible to start with a longer spark-gap, gradually increasing it, when finally a time will come when no pain will be produced no matter what the spark length.

By this method two effects are produced: a complete relaxation of the pyriformis muscle, and, to a greater or less degree, removal of the infiltration from the inflamed nerve. The patient who is assisted to the office for the first treatment is often able to walk out without pain.

In *acute cases* the treatments should be repeated twice daily. The early cases are often successfully treated with the wave current without recourse to sparks. There is no case of sciatica in which the process is only a simple inflammation, and in which adhesions have not taken place, that cannot be promptly cured by this method, and, when adhesions have occurred, the additional use of the X-ray and a great many static sparks to the site of the lesion will gradually effect absorption and a complete recovery. The worst cases may require from five to six months; but ordinarily cases of two or three months' standing will be cured in from one month to six weeks, and the acute cases should always be cured within ten days or two weeks. The writer bases these statements upon his own experience, not having failed, in upward of seventy-five acute cases, in curing them within two weeks, and many of them in less time.

Intrapelvic Neuritis.—In the sacroiliac cases the static wave current may be applied with a metal rectal electrode held in position against the nerve at or near the brim of the pelvis, over the place where these nerves cross the synchondrosis. In addition the local joint inflammation is treated as described elsewhere, q. v. In most cases this condition is promptly cured, only the chronic cases resisting the treatment.

Brachial Neuritis.—Brachial neuritis is one of the most common conditions which confronts the clinician, and one from which large numbers of people suffer uncured for years. Many cases of neuritis are complicated by a bursitis; and many cases of bursitis are mistaken for neuritis, i. e., inflammation of the subdeltoid bursa. The treatment of these cases is practically the same as for neuritis, when pain exists at the site of the bursa. There is muscular spasm in the muscles—pectoral, deltoid, and

other muscles of the shoulder in both cases. The application of the static wave current over the bursa and contracted muscles is effective in most cases in relieving the painful condition, but should be employed when chronic or resisting in connection with the application of the static sparks, until the movements of the arm at the shoulder are complete. An electrode of soft metal, 3 to 5 inches by 10, should be placed first over the shoulder midway between the neck and the outer border, extending from the clavicle in front backward over the scapula, for twenty minutes, then place it over the shoulder and upper third of the humerus in such a manner that one end lies over the belly of the pectoral muscle and the other end over the triceps back of the axillary space, for 15 to 20 minutes, the latter so long as any length of spark-gap causes pain. Full extent of movement will not be accomplished in chronic cases sometimes for weeks; but persistence both in the cases of brachial neuritis and bursitis will effect a complete cure of the condition in nearly all cases. In many cases in which the muscles are tense, and the condition has been of long standing, the application of mechanical vibration over the muscles and about the joint, as well as in the upper dorsal and lower cervical regions, will add very much to the relief and hasten the cure of the condition.

The *prognosis* in these cases, as in all inflammatory processes, as to time, is relative to the time the lesion has existed. The treatment should be administered until they are cured. After a time the treatments may be given on alternate days, but the sum total of treatments will be less in all cases if the treatments are administered daily. The prognosis as to cure is good in all cases when an ankylosis has not taken place.

Tic Douloureux.—Tic douloureux, so-called "facial neuralgia," is successfully treated by practically the same method as is employed in other cases of neuritis. In most cases, fortunately, only one of the many trunks of the nerve is affected, the most common being the branch which emerges from the infraorbital foramen. In other cases the inferior dental branch or the temporal may be involved. The lesion in most cases is fortunately at the site where the nerve emerges, and over these points the electrode should be pressed firmly during the treatment. The spark-gap should be at the start as long as can be borne, and lengthened very gradually as toleration will permit. It is the writer's custom to have the patient hold the metal electrode in position with the bare hand, the elbow resting upon the arm of the chair, during the administration. After the wave current, the writer's method is to apply the static brush discharge to the extent of inducing an active superficial hyperemia over the face.

Neuritis over the Cranium.—In neuritis over the cranium the only measure that can be applied satisfactorily is the static brush discharge. This, however, in this instance, is generally adequate, because the lesion is a superficial one.

Herpes Zoster.—This distressing type of neuritis is cured in most

cases in two or three days, when the patients come under observation at the outset. The application of heavy vibration with the ball vibratode along the intervertebral spaces of the involved branches, and the application of static sparks with the spark director to the same points, together with the application of the static wave current over the painful area, is promptly effective.

In *neglected cases,* when the herpetic eruption has developed, the application of the static brush discharge over the herpetic patches and over the surface generally, followed by an application of static sparks freely over the surface—it being impossible to use the wave current over these patches—the condition is promptly relieved and usually cured within a week from the outset. The patches disappear in most cases in three or four days. No greater satisfaction can be obtained from any method in therapeutics than from the treatment of herpes zoster, as here described.

Pelvic Inflammation

The treatment of non-infected inflammation within the pelvis, as found in conditions affecting the organs or parts of both sexes, as of the uterus and appendages in the female, and the prostate and vesicles in the male, and various more or less trivial though annoying inflammations of this type in the genitourinary tract, rectum, and bladder, are treated upon the same general principles employed in the treatment of the type of inflammation under consideration elsewhere.

The *technique of treatment* in these intrapelvic conditions requires the adjustment of properly applied electrodes adapted to the location, condition, and part to be treated, and a proper chair upon which the patient may comfortably recline.

Some prejudice has been created in the minds of clinicians against the use of glass vacuum tubes, owing to the fact that there have been occasional accidents from breakage of these electrodes. This, however, is a negligible quantity when the electrodes are carefully tested and found to be of firm construction.

The *indications* for the choice of metal or glass electrodes, when employed with the currents described, are practically as follows: The current from the metal electrode is more energetic, other things being equal, and the effects of the treatment more pronounced than from the glass vacuum electrodes. This, however, may be varied, as previously shown, by using terminal balls of different sizes upon the ends of the discharging rods—the smaller balls giving a softer, less intense mechanical effect. The advantage of the metal electrodes is that, when indicated, they do produce more positive effects. The metal electrodes for lightness should be made of aluminium and well polished.

The *wave current with vacuum tubes* produces relatively mild me-

chanical effects, other things being equal, and the electrodes are lighter and more easily made in shapes to conform to the various parts to be treated.

Dysmenorrhea.—Dysmenorrhea must be considered, as a rule, not due to stenosis, but commonly to spasm at the cervix; which the results of treatment demonstrate to be due to congestion in the muscular structures of the body of the uterus, the circulatory disturbance arising from various causes.

The method employed by the author was discovered quite accidentally by himself and his wife and associate, Dr. Mary Arnold Snow, when treating a case of constipation in which the obstructive cause was a retroverted uterus.

The *author's method of treating dysmenorrhea* was published in his first work on Static Electricity and Uses of the X-Ray and has since been published by him and others, who have become conversant with the method. In 1908 Dr. Edward C. Titus reported fifteen cases treated by this method with good results. Dr. Titus made the following observation:

"The uniformly happy results in the treatment of some fifteen cases during the past two years bear evidence of the help the advanced therapeutist is able to offer this unfortunate class of cases."

The writer and his wife and associate, Dr. Mary Arnold Snow, have since this discovery rarely failed in the cure of dysmenorrhea by this method, and have demonstrated the infrequency of an actual stenosis, and, furthermore, have, by actually curing a condition which has not been generally cured by other methods, been successful in curing the cases of hysteria in which this complication was present. These results have given strength to the opinion that it is at least one of the exciting causes of one of the functional neuroses.

Subinvolution.—Subinvolution, when not due to the presence of retained secundines or polypi in the uterine canal, is generally associated to a degree with relaxation, lost tone, and a condition of venous congestion and induration when not associated with the presence of infection. It is promptly responsive to treatment by the same method as that employed in the treatment of dysmenorrhea in all uncomplicated cases. When adhesions to the rectum or peritoneum elsewhere are found, generally associated with retroversion over the wall of the rectum, the current applied in this manner aggravates the condition. First employ surgical interference for the purpose of separating the adhesions, and then employ the static method.

In all other cases the static wave current applied, as previously described, is promptly effective, usually within two or three weeks.

Ovaritis and Ovarian Pain.—Except in cases in which an organic disease of the ovary exists, associated with either malignant or cystic disease, the presence of a complicating subinvolution or dysmenorrhea has been shown by the relief and cure of these conditions to have been the cause. It is very rarely that this symptom is found, except there is present one or another of the forms of uterine congestion, infectious or

non-infectious. Where the pains are severe and persistent, and there is a certainty that no infection is present, the wave current may be applied directly over the region, or, when in doubt, the direct d'Arsonval current for the induction of localized hyperemia will in many cases relieve the symptom of pain; and the regional muscular spasm usually associated with it. There are very few cases of local ovarian pain that cannot be cured by one or another of these procedures, one or more of which should always be employed prior to performance of any contemplated operation. When these methods are generally recognized, they will be adopted by the gynecologists; then surgery will be rarely resorted to in these cases.

Infiltration or Congestion of the Meatus of the Female Urethra.—These conditions are promptly relieved by the employment of the vacuum tube wave current, first employing as large a vaginal electrode as can be passed, held firmly against the urethra with an X-ray tube holder, and later using a urethral electrode as large as will pass, inserted into the urethra. The treatments should be administered daily for at least fifteen minutes.

Urethral Caruncles.—Urethral caruncles partake in most cases of two conditions: (1) a hyperplastic growth, and (2) an associated infiltration. The treatment should be the same as in the preceding condition up to the point of relieving the local pain and congestion which are usually present. To remove the caruncle, however, requires the employment of a more active measure, as of destructive fulguration or the negative pole of the constant current, or surgical removal. If either of the latter methods is employed for the removal, a congestion of the meatus will follow the destructive treatment; in order to overcome the consequent infiltration and prevent reformation of scar tissue, treatment with the vacuum tube wave current should be resumed until the reaction subsides.

Hemorrhoids.—Hemorrhoids in the early stages, resulting from obstructive circulation of the liver, or constipation, are very promptly relieved and the distressing pains and tenesmus arrested by the application of the vacuum tube wave current with the electrodes designed by Dr. Arnold Snow. An electrode which will pass without causing too much discomfort is placed in position and pushed firmly up against the anus, in order to affect any external or protruding piles present. The shoulder of this electrode is designed for the treatment of these cases.

Fissure in Ano.—Fissure in ano is treated in practically the same way as hemorrhoids, though at first a very small electrode is passed. The relief from this treatment is instant; and, if the bowels are kept loose for a week, the infiltration is softened at the margins of the fissure, and the surfaces heal together in a few days. There is probably no more simple method of treating a very distressing affection than the treatment of fissure in ano by this method.

Spasms of the Sphincters.—Spasms of the various sphincters are promptly overcome by the employment of the static wave current or vacuum tube wave current in the method described. There is no other measure that compares in efficiency with the passage of electrodes, gradually increasing the size for the relief of spasm of the sphincters, including vaginismus.

Spasm at the Sigmoid.—Spasm at the sigmoid is relieved on the same principle. It requires, however, a specially formed electrode to successfully reach the sigmoid. The author has employed the electrode which is so curved that, by rotating it as it is inserted, it readily passes into the sigmoid. First pass the electrode through the sigmoid past the spasm, and then gently draw it down until the constriction is felt. After ten minutes it may be drawn farther down and the current be continued for ten minutes longer. The employment of this method is often of value in relieving stubborn cases of constipation due to spasm at this site, q. v.

One case of constipation, which the author had under treatment for upward of two months with indifferent results, yielded promptly and permanently to three applications of the wave current at this site. It is very difficult to make a diagnosis of this condition, except by the employment of this electrode, when the spasm will be readily appreciated, the final demonstration of its presence being the result of subsequent treatment. The same method can be employed in the treatment of spasm of the esophagus by attaching a small ball to a flexible wire, and having the patient swallow it, when the current can be gently turned on. As it drops down into the stomach, it can be returned to the cardiac orifice or other place of spasm by drawing the cord upward and holding it there, again applying the current. The wave current is also employed for overcoming muscular spasms of the gastrointestinal tract, employing the flat metal electrodes, relief being almost instant with the turning on of the current.

Muscular Spasm at the Internal or External Abdominal Ring.—Muscular spasm at the internal or external abdominal ring, contracting about the cord, is relieved by the wave current. This is best accomplished by bending a piece of 22 gage composition metal so that the convex surface rests against the site over the canal, the patient holding it in position with a towel, when the current will not pass through the thickness of the towel to the hand. The author employs this method in the treatment of varicocele, the varicosity disappearing in most early cases.

Prostatitis.—Prostatic enlargement may arise from various causes. The most common condition presenting, however, is one of infiltration. The infiltrated prostate usually presents on examination a boggy feeling, and is often very tender to the touch. In some cases, however, in elderly men the condition may have become subacute, and will very closely resemble the feeling of a fibroma. It is difficult in these cases at first to

differentiate; but under treatment the rapid reduction in size, with softening by the first application of the wave current, will make the diagnosis of infiltration certain.

If a condition of *malignancy, tuberculosis,* or *calculi* is present in the gland, the condition will be aggravated by the application of the wave current, which will be manifest at the first or second treatment, and will contraindicate the employment of the method.

Gonorrheal prostatitis should be treated in the same manner as the other cases, because the germs are expelled by the mechanical effects of the current. In a few cases in which the veru montanum was involved, extending anteriorly or forward in the deep urethra, it is not always possible to effect a complete relief from vesical disturbances, though the body of the gland is reduced practically to normal.

The author's method of treatment, which was discovered by him more than ten years ago, is employed as follows. The patient is placed upon his side upon the static chair with a pillow or folded sheet under his hips. The electrode is put in position and maintained there either by the hand of the patient, or by the method at present employed by the writer—held in position with an X-ray tube holder. This treatment is continued for twenty minutes. In the cases of acute sensitive prostate, the spark-gap at the outset tolerated will be from one inch to an inch and a half, and sometimes even less. The spark-gap should be lengthened gradually as in the treatment of neuritis and other inflammatory affections, as the patient will tolerate the increase. In acute cases it may not be possible to increase the spark-length to four or five inches during the administrations within the first week, though in most cases at the second or third treatment it will be possible to open the spark-gap to three or four inches at the outset. In the acute cases the prognosis is always good for a prompt recovery, with a cure of impotence and great relief from reflex nervous symptoms—sexual neurasthenia—so commonly associated with this affection. In some cases, in which the gland is very sensitive, it may not be possible to pass an electrode past the gland at the commencement of the first treatment. In such cases the electrode should be held in contact against the lower end of the gland, when, after five minutes, the machine may be stopped and the electrode passed a little farther, repeating this two or three times during the first treatment, or until it passes freely into the rectum. It is rarely difficult to pass the electrode at the outset of the second treatment even in these acute cases. Care should always be taken that the electrode and handle are in line with the axis of the body, so that the electrode will surely lie in the median line against the two lobes.

The *rate of discharge* at the spark-gap should be regulated not to exceed 300 per minute. This is a matter of no small importance in the treatment of all infiltrating processes, or for the relief of muscular spasm. The treatment is administered daily for from five to ten days and then on alternate days until the gland is normal. This will be effected in the early cases in about one month. In cases of long standing it may take much longer. Except where the cases are actual hypertrophy of the tissue elements, the gland even in advanced years may be reduced to normal size.

This method of treating enlarged prostate is commended by the writer, who has been successful in more than 200 cases, and his experience has been confirmed by many other observers in recent years; the results indicating that the operation

of prostatectomy should never be resorted to until these simple, harmless, and efficient methods have been first tried.

Vesiculitis.—Vesiculitis very often complicates prostatitis. Whether of simple or specific origin, the treatment is practically the same as for prostatitis, and is effective within a reasonable time. The cylindrical electrode is placed high enough to come in contact with the vesicles, and the treatments are administered in the same way as in the treatment of prostatitis until the condition is relieved.

Visceral Congestion.—Visceral congestion, including non-infectious inflammatory conditions of the liver, spleen, pancreas, kidneys, stomach, and intestinal tract, are all amenable to the same principles of treatment as infiltrations elsewhere, it being important in all cases to differentiate the presence of infection or malignancy.

Cirrhosis of the Liver.—*Hypertrophic* cirrhosis of the liver is remarkably benefited, and the symptoms associated with the conditions satisfactorily relieved, by the application of the wave current directly over the enlarged liver. It is remarkable how promptly softening and reduction in the size of the liver take place with improvement of symptoms. A large sheet metal electrode is applied directly over the hypertrophic liver in the abdomen, and a slow discharging spark-gap from six to twelve inches in length, according to the effects upon the patient, is employed. The length of spark-gap demanded will vary according to the sensitiveness of the liver and the thickness of the fat over the abdominal muscles. The treatment will not be of permanent avail, obviously, in patients who persist in their alcoholic habits.

In the *atrophic* stage of cirrhosis the wave current or, perhaps better, the direct d'Arsonval current and radiant light and heat will stimulate the liver to better efforts, and in some cases markedly diminish the ascites.

Splenic Hypertrophy.—In splenic hypertrophy due to malarial causes the wave current applied as in the treatment of cirrhosis is very effective. The spleen may be practically reduced in a few weeks to its normal size, and the relief of the patient from various symptomatic conditions will be remarkable. In one case in which this treatment was employed by Dr. Condict in India, a condition of hemophilia from which the patient had long suffered was cured with the reduction of the splenic hypertrophy. This was a remarkable case, in which the woman, in carrying out a native custom of cleaning her teeth and gums with charcoal as part of the morning ablutions of the natives, produced profuse hemorrhage every day on each occasion, which ceased after the reduction of the spleen by the static wave current.

Diabetes Mellitus.—In diabetes mellitus the writer and his confrères have had satisfactory results from the application of the wave current to the pancreas,

marked in the cases which were not complicated by hypertension. A metal plate electrode about four inches square is placed over the epigastrium, and a spark-gap used as long as the patient will take without too much discomfort. The improvement is often prompt in these cases and, while it is not a specific, it is as a rule beneficial and absolutely harmless and unobjectionable in all cases, and offers another means of relieving this grave condition. In cases with hypertension, the reduction of blood pressure by the auto-condensation method has frequently caused the glycosuria to absolutely disappear. The writer has verified reports of so many cases of cures by this method that it seems to be indicated in every case of diabetes complicated by hypertension.

Nephritis.—In *parenchymatous* and *interstitial* nephritis the application of the static wave current daily over the kidneys is one of the most effective means of restoring the functions of these organs. Bearing in mind that the kidneys lie just beneath the muscles on either side of the spinal column, they are very accessible and readily affected by this method. Apply an electrode six by eight inches directly over both kidneys, bridging the spine. If the spinous processes are prominent, an electrode may be placed over each side, and the two electrodes connected to each other, treating both kidneys at the same time. The usual rule of employing a long, slowly discharging spark-gap is observed in these cases—a spark-gap of eight to twelve inches, varying with the physical conditions of the individual. The writer has obtained in several instances complete disappearance of granular and hyalin casts and albumin. It is a far more efficacious procedure than the removal of the capsule, and the promptness with which relief takes place in the stages favorable to treatment by any measure is remarkable.

In *parenchymatous nephritis* the employment of the static wave current and body light baths daily will obtain remarkable results, and in many cases effect a cure, particularly in young adults.

When interstitial nephritis is complicated, as it usually is by hypertension or a failing compensation in the later stages, great benefit is derived from the employment of d'Arsonvalization. These methods have been tried and not found wanting.

Constipation.—Constipation arising from numerous causes, functional, spasmodic, and obstructive, must be treated with a view to relieving every causative factor in each case, because in most instances one condition leads in succession to another; and the general symptom-complex in each case is one of intestinal atony, colonic impaction, with deficient secretions, and a vicious habit of irregularity in attending to the demands of nature, with the employment of cathartics, and errors of diet.

The electrical treatment may consist in applying the static wave current with a large metal abdominal plate electrode over the abdomen with as long a spark-gap, slowly discharging, as the patient will take without inducing muscular cramp or pain, the application to be continued for

twenty minutes. Another method is to place a metal electrode in the rectum, and an abdominal plate over the abdomen, connecting one side to one pole of the static induced current, and the other electrode to the other pole. The current should be administered for twenty minutes with a slowly discharging spark-gap, which will produce positive deep muscular contractions during the administration.

Another method which employs the *sinusoidal current* is to place a metal electrode in the rectum, and apply over the abdomen the electrode with the multiplex sinusoidal current, q. v. This should be continued for fifteen or twenty minutes, thoroughly exercising and arousing the muscles over the whole abdomen by moving the electrode about in the hands of the operator. These methods are effective in arousing atonic and relaxed conditions of the viscera and of the abdominal wall, and at the same time restore the functions of secretion.

In addition, the systematic regulation of diet and exercise, with the institution of habits of regularity in going to stool, is effective in variable combinations as indicated; in most cases not only restoring the tonic conditions of the alimentary tract, but also establishing normal function.

In obstructed cases it may be necessary to treat a retroverted uterus or enlarged prostate or a spasm of the sigmoid or anus, q. v., in order to still farther facilitate the cure of the condition.

Cardiovascular Diseases

There is no field in electrotherapeutics where greater success attends the effort than in the treatment of cardiovascular diseases, when the etiological factors are recognized and corrected—namely, the correction of habits of diet, with the regulation of the food intake and the physical exercise of the patient. When these patients are put upon first a non-stimulating diet excluding all animal proteids, including eggs, together with the correction of other alimentary irregularities, the control of the condition of hypertension by d'Arsonvalization is effective in all cases except those of advanced arteriosclerosis, in which the arteries have become generally sclerosed.

The *sphygmomanometer* in the hands of the clinician in conjunction with the d'Arsonval method of treatment has demonstrated the positive effect of this current properly administered in lowering and controlling arterial hypertension. The methods of d'Arsonvalization employed in these cases are either the autocondensation or autoconduction method. Autocondensation is administered upon a suitable couch or table. A cushion approximately three inches in thickness, six feet long, and twenty inches wide, made of sheets of felt, silk waste, or other non-conducting material, covered with a non-conducting material, as pantasote, corduroy, or other cotton, silk, or woolen fabric, is placed upon the chair. The

sheet of metal, about four inches shorter and four inches narrower than the cushion, may be secured to the chair seat or placed loosely beneath the cushion. The d'Arsonval current is administered with one terminal of the d'Arsonval solenoid attached to the metal beneath the cushion, and the other by a bifurcated cord to two metal handles, or a single cord to one longer handle. The hot wire meter should indicate 400 to 600 milliamperes, according to the capacity or size of the individual, and should be continued approximately for 12 minutes at each treatment. This, in the writer's experience, constitutes a dosage which uniformly lowers

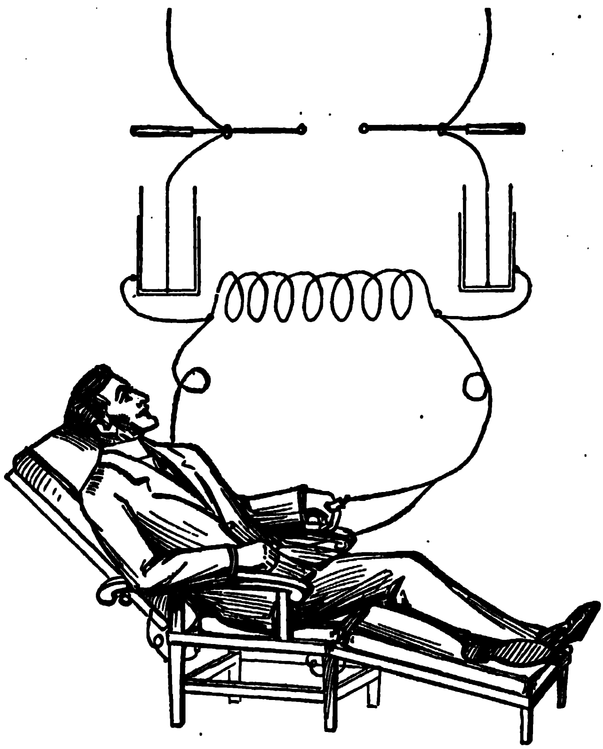

FIG. 12.—THE AUTOCONDENSATION METHOD.

blood pressure from ten to forty millimeters of mercury; usually ten to twenty millimeters at each sitting, the pressure in the interval increasing a few millimeters, but falling day by day, either on daily or alternate day treatments, to a substantially lowered tension—in early cases to normal. The lowered tension may be maintained in most cases either by regulation of diet and exercise, or in addition may require an added occasional treatment once weekly or once in two weeks, and in some cases with longer intervals between treatments.

In cases with low and failing blood pressure with edema, where com-

pensation is failing, there is no contraindication for autocondensation treatment; but, on the contrary, everything that can be done to relax tense arterioles under these conditions favors the condition of the heart by diminishing its labors, with resulting marked improvement in the condition of the patient. It must be understood that d'Arsonvalization in no way depresses the heart, but diminishes its labor.

In *angina pectoris* for the same reason lessened tension relieves the labor of the heart, with prompt relief from pain and dyspnea. In con-

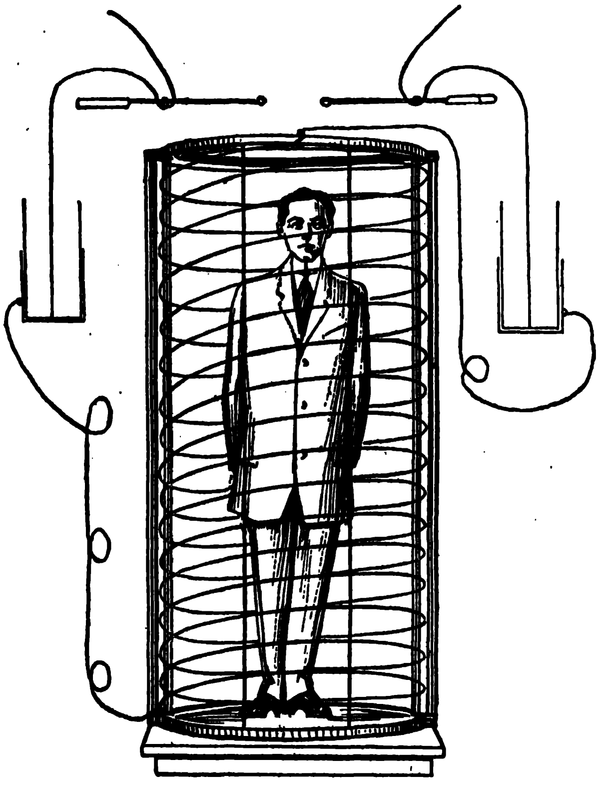

FIG. 13.—THE AUTOCONDUCTION METHOD.

ditions of valvular incompetence with hypertension the relief is positive from the outset. The following case well illustrates the effects:

Mr. A., a patient 45 years of age, had been confined to his bed for months with pulmonary edema, having had three pulmonary hemorrhages, and a constant cough. This patient was suffering from mitral insufficiency with hypertension. When he reached the office his blood pressure was 212 mm. His pressure within a week, with alternate day 12-minute autocondensation treatments, employing 500 milliamperes of current, had fallen to 155 mm., the dyspnea and cough had disappeared, and under

corrected diet and regulated exercise, with alternate day treatments with autocondensation, the patient made a complete recovery. His pressure is now maintained at 140 mm. or less, with an autocondensation treatment once in two weeks without the administration of any drug, but strict attention to diet, avoiding all animal food, including fish and eggs, and any excess in quantity of food consumed.

The autoconduction method is effective in the treatment of these cases. The writer, however, has used the more convenient and fully as effective method of autocondensation.

Properly constructed resonators connected with Ruhmkorff coils, static machines, or other high potential transformers, are always effective in producing the requisite current for the treatment of these cases. Likewise, the alternating current transformers referred to in previous cases are proving efficient in the treatment of hypertension and arteriosclerosis.

Spinal Cord Diseases

In the early stages of most affections of the spinal cord electrical treatment, in combination with other indicated medication or habit of exercise, meets with a large measure of success. The general principle of treating cord affections must depend upon three principles: (1) the removal of local infiltration or congestion of the meninges, which are causing pressure upon the cord; (2) the restoration of normal metabolism in the substance of the cord; and, (3) where a syphilitic condition is positively demonstrated, the employment of an indicated mercurial or other treatment in connection with the electrical treatment.

Electrical application to cord conditions consists in the administration of the static wave current directly over the lesion of the cord. It must be fully appreciated that, in order to affect the meninges and structure of the cord, a very long spark-gap with the wave current is imperative. We therefore apply an electrode not more than 1¼ inches in width, and, in cases involving the whole length of the cord, from 16 to 22 inches in length, according to the patient. Whenever a spark-gap of this length is used, even in young people, it cannot be expected to accomplish positive effects upon the cord without the employment of a very long spark-gap—at least ten to fourteen inches in length, which requires a Holtz machine of large efficiency. In cases in which a marked effect is demanded even this long spark-gap should be applied with a shorter electrode first over one half and then over the other half of the cord.

The *modus operandi* of the wave current in these cases is that the current passes, as in all cases, to surround the body during the period of charge, and that, when the current breaks to discharge across the spark-gap, it rushes with great velocity, converging to the metal electrode from all parts of the surface, out through the spinal cord and bones of

the spine, as graphically indicated in Fig. 7. It is physically well demonstrated that this effect must follow. The current in discharging produces profound effects upon the structures of the cord, effecting drainage from infiltration, and improving the metabolism of the structures, as in the treatment of other inflammatory conditions. These effects are fully verified in the therapeutic results obtained in the treatment of spinal cord affections, and justify their thorough trial, at least by even those who may be skeptical, and their adoption by all. The writer's experience includes the treatment in this way of the following conditions in which positively beneficial results and many cures have resulted, as will be indicated when considering each of the conditions:

Tabes Dorsalis.—Tabes dorsalis, when of non-specific origin, will in most cases respond to be arrested; and also when complicated by syphilis, if the treatment is employed in connection with specific treatment. The long spinal electrode is applied as described, and the treatment administered for twenty minutes, at first daily, and later on alternate days. This is immediately followed at each treatment by the application of static sparks and friction sparks thoroughly as follows: The application of friction sparks, employing the pear-shaped ball electrode rubbed over the clothing over the anesthetic areas which are marked in nearly all cases on the legs, below the knees. Apply the friction sparks to these regions with rapid movements. The patient may at first barely feel the sparks; but, as it is continued after a time, will complain that it is too hot, indicating the awakening of the sensorium. The patient remarks the increasing sensation in the limbs; for, to a considerable degree, the treatment does restore the sensation of the parts. In the same manner the friction sparks over the stockings, if thick and not damp, or through a thickness of flannel, should be applied over the soles of the patient's feet, the increased sensation here improving the locomotion of the patient for obvious reasons.

Wherever pains are annoying the patient the sharp application of hundreds of short sparks to the area will practically arrest the pain. This application to the painful regions of hundreds of small sparks is most grateful to the patient, and of emphatic therapeutic value for that purpose. The application of long sparks, employing the spark director in the intervertebral spaces up and down the spine, adds another valuable feature to the treatment of these cases. The results from the static treatment of locomotor ataxia are satisfactory in nearly all cases.

Pachymeningitis.—Pachymeningitis in the early stages is relieved, and with surprising promptness, by the application of the static wave current over the spine.

Traumatic Myelitis.—Traumatic myelitis or contusions resulting from accidents, with more or less involvement of the joints surrounding the cord, are practically relieved in all cases in which fracture of the bones

or laceration of the cord has not occurred. It was in this class of cases, when treating a very heavy patient who had been injured in a railroad accident, that the writer was able to confirm without question the effects of the wave current in relieving deep-seated congestion of the cord and meninges. The case, which had made no improvement for two weeks under rest, was promptly relieved and cured in a few weeks after the institution of this method of treatment.

Poliomyelitis.—There is probably no one affection in which the effects of the wave current applied to the spine are more promising than in the treatment of poliomyelitis. The notion that these cases should not be treated with electricity until after several weeks is fallacious as concerns the static current. Even in the fever stage, when these young patients can be brought to the static machine, and the current applied to the spine, the improvement is prompt from the first treatment; and the improvement is progressive; and, in the writer's experience, in nearly all cases who are brought under treatment in the first days or week following the paralysis a complete recovery is made.

It has been demonstrated to the writer, in every case that has come under observation where the treatment has been delayed even for weeks, that the improvement following the institution of treatment is immediate. In observations made on the treatment of many cases of this affliction the writer has seen uniformly good results and marked improvement, except in cases that have been neglected for more than six months; and in some of these the improvement has been very considerable.

Another method used in conjunction before or following the spinal treatment, when improvement is delayed, is the exercise treatment, which the writer has recently discovered to be a very valuable aid in bringing the atrophied muscles gradually into activity. The method is as follows: Either a long, narrow spinal electrode is applied over the spine, or a large indifferent electrode on the back, connected to one side of the machine for the static induced current; and small metal electrodes are applied and secured in position to some part, usually the middle, of every atrophied muscle. These are each connected by short wires to a common wire, which is attached to the opposite pole of the static induced current. The spark-gap is then regulated to the toleration of the patient, and the discharge at the spark-gap to a rate of about 120 per minute. At first these treatments should be for not more than ten minutes, usually increasing the time up to twenty minutes in subsequent treatments, as the muscles become more used to the exercise. This method is far more practical than the method of applying wet sponges and stimulation with the constant and induced current; a treatment with which, in most cases, the spinal cord condition has been ignored.

Spastic Paraplegia.—Spastic paraplegia is treated in very much the same manner as the other cord conditions, the wave current being applied directly over the region of the cord, where manifested by the lesion. In late cases the relief of the condition of muscular spasm and

contraction, together with the improvement and control of the sphincters, usually results from twenty-minute daily or alternate day treatments.

In early cases complete recovery has occurred in cases which warrant the giving of a fairly good prognosis when the treatment can be instituted at the outset. When syphilis is indicated by a positive Wassermann reaction, antisyphilitic treatment is also indicated.

Chorea.—In chorea the method to be employed is quite different, the static wave current or any current which produces noise or sensible pulsation tending to aggravate the condition. The application of the static current is, therefore, made in these cases with the patient lying upon the back with a long spinal electrode next to the spine, and the sliding rods widely separated so that no sparks will pass. Under these conditions the static machine should be run at a fairly high rate of speed. The application of radiant light baths, the elimination of all animal foods from the diet, careful attention to the alimentary canal in all particulars, and the removal of all irritating environment from the life of the patient, with fresh air and life in the open, efficiently relieve these cases when not of too long standing.

Functional Neuroses.—From the writer's point of view and success in the treatment of hysteria, and neurasthenia, and cases of dementia precox and delusional insanity, he believes that a more careful study of the *symptom-complex* usually associated with these conditions will reveal a physical cause in most cases. Prostatitis, dysmenorrhea, ovaritis, constipation, and autointoxication, when treated with the methods given in these pages, have been effective in curing so many of these sufferers in the early stages that it seems incredible that any branch of the medical profession should deny the physical cause of derangement.

It seems that the proper management of these cases looks to the conjoint employment of autosuggestion for its psychic influences upon the patient and the correction of physical defects as well. The writer has become convinced from his observation and experience that the cure of physical defects is essential in all cases. The differentiation of variations in the symptom-complex as presented in the clinical pictures of neurasthenia and hysteria is sometimes difficult. Gowers expressed the same differential view in an early edition of his work, when he said that it was largely a matter of sex. Freud has shown clearly the relations of sexual influences as affecting or causing psychopathic states, but has not associated them as we are bound to with pelvic derangements. The cure of many patients not relieved by suggestion or drugs, but responding to treatment of pelvic conditions, has demonstrated, at least, that functional neuroses often originate from physical causes.

More than 25 per cent. of 180 cases of prostatitis that the writer has treated have been neurasthenics; and, with the exception of two of these cases, the nervous symptoms have disappeared during the treatment. With hysteria the results have been very much the same. Few early cases of hysteria in young women, complicated by dysmenorrhea, are not entirely cured with the relief of the local condition.

CHAPTER IX

RADIANT LIGHT AND HEAT THERAPY

WILLIAM BENHAM SNOW

The therapeutics of radiant light must include the effects of radiant heat; because radiant energy emanating from any source of the higher and lower frequencies is transformed into heat when it comes in contact with any body or objects which absorb it. In other words, as radiant energy impinges upon the human body, penetrating the tissues, a transformation takes place of radiant energy into heat units so far into the tissues or substance as the radiations penetrate.

We commonly consider the solar spectrum as composed of the visible spectrum, which is light, and the higher frequencies—the ultra-violet—and the lower frequencies—the infra-red. Properly, then, only those frequencies are light which, when impinging upon the retina, produce the sensation of sight.

In a treatise on the therapeutics of radiant energy, however, it is necessary to investigate all the frequencies of the spectrum, visible and invisible, and to consider their effects. It is the writer's purpose, therefore, to speak of the subject broadly as radiant light and heat, the heat not being limited in its source to the infra-red or heat rays, but being produced also by the luminous rays of the spectrum, and, to a minute degree, by the ultra-violet as well. All of the frequencies, therefore, produce heat in varying degrees by transformation of radiant energy into heat units.

PHYSICAL PROPERTIES OF RADIANT ENERGY

Light is a manifestation of energy transmitted through space and capable of producing effects upon the retina of the eye by which other objects are rendered visible.

Frequencies.—The various frequencies of light and the invisible frequencies of the ultra-violet and infra-red are to be considered relatively, according to their various wave lengths and frequencies. The range of the visible spectrum extends between rates of vibration approximating

450,000,000,000 per second for the red, and 750,000,000,000 for the violet. The ultra-violet represents frequencies which extend into billions of billions, while the infra-red extend far below the frequencies of the visible spectrum. The physical properties of these radiations, as affecting the retina and chemical substances, as nitrate of silver, vary with the frequency and the wave length. The end of the spectrum to which the silver salts are most susceptible is the ultra-violet. The orange, red, and infra-red do not affect appreciably the silver salts. For this reason the higher frequencies have been designated the chemical rays, which is true, but in a sense misleading; because the other frequencies produce chemical effects also, as the effects associated with heat production; or, as Oliver Lodge has said, "some affect other substances."

Penetration.—With these various frequencies the penetration is as the wave length, and the heat production inversely as the frequency. In other words, the thermic effects of the higher frequencies are practically nil, while the thermic effects of the infra-red and lower frequencies are very marked.

The penetration of radiant energy from luminous sources varies in depth with the character of the substance and the wave length of the various frequencies. It penetrates, according to Kellogg, at least six inches within the human body. It is readily demonstrated that the luminous rays, particularly the red rays, penetrate through bone and other tissues of density by the illumination of the antrum by placing a small lighted incandescent lamp in the mouth, or by illuminating the frontal sinuses by shielding the light held in the inner angle of the opposite eye.

Finsen demonstrated that ultra-violet rays did not penetrate to any extent a vascularized tissue, acting only superficially. His experiment consisted in exposing one surface of his wife's ear, against the opposite surface of which was placed a sensitized film, to a powerful ultra-violet radiation, when the film was not fogged. This demonstrated the impenetrability of that very translucent, almost transparent, tissue. After bringing sufficient pressure to bear upon the ear to devascularize it, however, the ultra-violet rays passed readily through and fogged another film. By this experiment Finsen demonstrated the necessity of rendering the tissues anemic by pressure or the local administration of adrenalin in connection with the treatment of lupus. This experiment proved, furthermore, the inadequacy of the ultra-violet rays in therapeutics except under the conditions employed by Finsen, or when it was desirable to effect a superficial hyperemia.

Refraction.—When a beam of light passes through media of varying densities it is bent out of its direction, both at the entrance to the denser and the exit into the rarer media, being bent in the first instance at an angle from the perpendicular and in the latter toward the perpendicular

drawn to the plane of the surface of the glass or other medium through which the rays pass (Fig. 1).

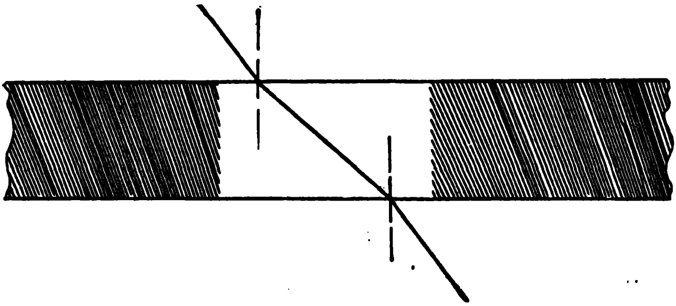

Fig. 1.—Illustrating Refraction.

It is by refraction through a prism that the various colors of the solar spectrum are shown, a pencil of light falling upon the prism being

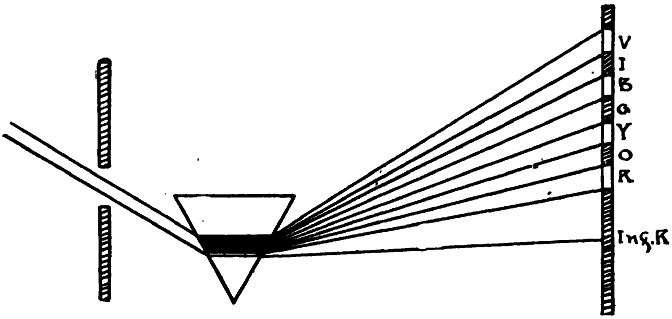

Fig. 2.—Showing Refraction of a Beam of Light Passed Through a Prism, and the Order of the Spectral Colors.

thus refracted at varying angles; in a darkened room showing the seven prismatic colors in the order as indicated in Fig. 2.

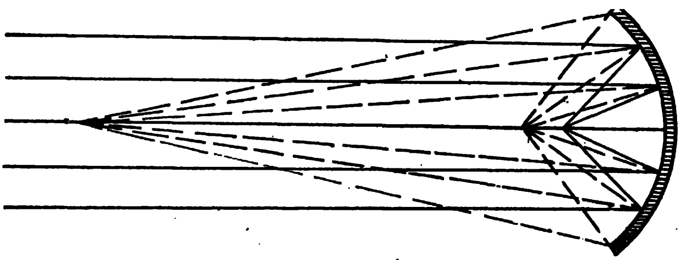

Fig. 3.—Showing Reflections in Parallel and Convergent from Concave Mirror.

Reflection.—Reflection is the property of radiant energy whereby, when thrown against a smooth or polished surface, it is reflected at an angle according to the obliquity at which the rays strike the reflecting

surface, the angle of incidence being always equal to the angle of reflection. Reflected radiations from concave surfaces of mirrors or polished metal, when projected against such parabola, may be reflected to a focus. The position of the focal point will depend upon the distance of the light from the reflecting surface and the concavity of the parabola; i. e., the arc of the circle of which the parabola is a segment (Fig. 3). The focal point may be changed respectively by moving the luminous object farther from or nearer to the reflecting surface, thereby rendering the radiations more or less convergent, parallel, or divergent. This is made use of by varying the focus of the marine searchlight and in other arc lights used for therapeutic purposes.

It should be borne in mind in the employment of therapeutic lamps that, if the focal point crosses between the parabola and the object illuminated, the light when projected upon a screen will appear as a ring of light surrounding a dark spot, as indicated in Fig. 4. Within this

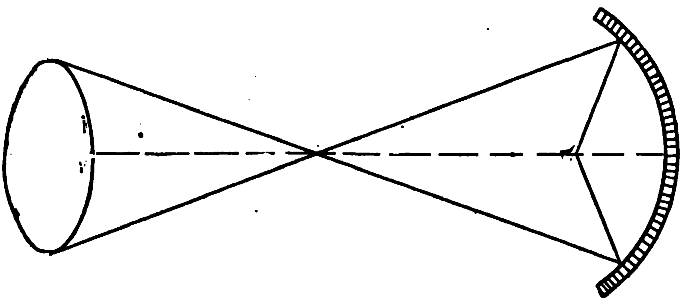

FIG. 4.—INDICATING CROSSING OF CONVERGENT RAYS AND DARK SPOT BEYOND, WITHIN WHICH SHIMMER APPEARS.

circle of light a violet color will appear, which has misled many observers who were not informed to believe that it was the violet radiations within which were the ultra-violet, whereas it is but a reflected shimmer and not of value for therapeutic use. No one should be led unsuspectingly to believe that this phenomenon is an ultra-violet radiation.

In order to investigate the practical value of an apparatus, inquiry should be made with reference to where the focal point will fall, with the understanding that immediately beyond the focal point the rays are dispersed in such a manner as to be of little value for therapeutic purposes. The form of the parabola relative to the position of the light, therefore, requires particular attention. The small lamps will be shown to be of not nearly so great efficiency as the lamps having a reflecting surface measured by an arc of a longer radius. With the incandescent light provided with a parabolic reflector the place of greatest intensity is naturally at the focal point. If this focal point is far out from the rim of the lamp, the therapeutic value of the lamp is greater, because the radiations

within the focal point are of greater practical value and utility than when it is nearer the rim of the reflecting lamp.

Polarization.—Polarization is of no importance as concerns the therapeutic employment of light.

Fluorescence.—Fluorescence is induced in certain substances from the projection of radiant energy against the surfaces, some of which are capable of absorbing and again transmitting the energy after the exposure is discontinued. Sulphid of calcium continues to fluoresce for hours after prolonged exposures to light; and it is possible that some of the therapeutic properties of sulphid of calcium may be due to this quality of fluorescence. It is worthy of experimentation to investigate whether long exposures of sulphid of calcium to light before administration do or do not add to its therapeutic value. Otherwise, as circulating in the blood it is more or less exposed to light in the exposed parts of the body, which, on account of its fluorescent qualities, may explain its effects as claimed upon streptococcic and staphylococcic infections.

Color.—Color is the expression as conveyed to the retina by the different degrees of refrangibility of the visible spectral rays. The term light has been employed by some writers to all of the radiations of the spectrum as well as to the X-ray. This is properly a misnomer, as only the visible frequencies constitute what is recognized as light.

The physical properties enumerated include the actions or effects of radiant energy when projected upon substances other than the human organism.

Effect on Germ Life.—Another property of radiant energy is its effect upon germ life as present in the atmosphere and running water. It is very remarkable how promptly these microorganisms are destroyed by the influence of radiant energy; which is probably due largely to the action of the ultra-violet rays, which penetrate both air and water. It has been demonstrated that water, taken from sewage sources, loaded with bacteria, is made practically free of these living organisms by the passage of sunlight through them. This, however, must be done with the surfaces exposed, as the ultra-violet rays do not pass through glass. This demonstrates that it is the ultra-violet rays that destroy germ life.

It is remarkable, furthermore, that in the vicinity of large towns and cities, where the air is full of organic matter, the percentage of ultra-violet radiations that reach the earth is remarkably small, their energies having been exhausted upon the organic matter in the atmosphere. It is the property of these higher frequencies by which they effect the destruction of germs that renders the air of the country so healthful and free from germ life, and also that destroys the germs in running water exposed to sunlight.

The ultra-violet rays are, therefore, one of the most useful energies of Nature, and it is not surprising that many therapeutists have looked to

these higher frequencies for other great therapeutic benefits. When applied to the human organism, however, they do not act to produce effects so beneficial as the action of the penetrating frequencies, which actively increase metabolism and produce other effects which are valuable.

For some time observers have recognized injurious effects of the higher frequencies upon the eyes, which are not so marked in the cities as in the clear air of the country and at sea. Glasses, because they absorb these rays, protect the eyes from these effects.

Tanning of the Skin.—There are certain other physical effects of radiant light and heat which are properly peculiar to animal organisms. As the chemical actions of light facilitate the induction of oxidation of organic substances in the air and water, so we would anticipate that they would have like antiseptic effects when applied to the body. On the contrary, as has been previously shown, the higher frequencies do not penetrate except to the outer layer of the true skin, where they act as irritants, producing profound superficial hyperemia, which results in desquamation and tanning.

Tanning of the skin is an effect almost, if not entirely, due to the ultra-violet rays, a pigmentation taking place beneath the epidermis. This is undoubtedly a beneficent process, producing, as it does, a protection to the underlying structures when exposed to the penetrating luminous rays of the sun.

It is not improbable that races that have lived for generations within the tropics have become dark skinned through the influence of discoloration produced in this manner, succeeding generations becoming darker and darker in the process of time. That the dark-skinned races suffer less from the exposure to the sun's rays is a well-known fact. Wilkinson has frequently called attention to the unfavorable conditions of the tropics for the white man. It has now become a custom for educated white men who understand the principle, when living in the tropics, to wear colored underclothes for protection of the body, except the hands and face, from the influence of the sun's rays.

The tanning of the skin by the ultra-violet rays is the very action which contraindicates its employment in therapeutics; for, when we wish to make frequent and long applications of radiant light and heat for its effects upon metabolism, the tan of the surface prevents the penetration of the radiations within the organism. For the same reason, radiant energy is far less effective when employed in the treatment of dark-skinned individuals—brunettes deriving apparently little benefit from its employment, except from the effect of increasing perspiration.

Dark-skinned races, and other individuals having dark skins, perspire very profusely under prolonged exposures to the sun's rays, the penetration producing a cooling influence in dry climates, due to the latent heat of evaporation. It is owing to this that the endurance of the dark-skinned

races in the tropics is so great, the body being kept cool by evaporation of the perspiration.

Production of Hyperemia.—Hyperemia is produced by the various frequencies as follows: (1) The irritating effects of the ultra-violet radiation upon the outer layer of the corium and epithelium induce a very intense superficial hyperemia. Otherwise the action of radiant light in inducing hyperemia is due to the heating of the tissues by the combined influence of the luminous and invisible heat rays. Whenever the temperature is lowered or raised in a part, the vasomotor mechanism responds to send an increased supply of blood to the exposed tissues to maintain equilibrium of temperature. Taking advantage of this principle, the employment of prolonged applications of radiant energy, which penetrates for many inches into the tissues, not only heats the surface but all tissues into which it penetrates. It is this principle of physiological action upon the physical mechanism of the human organism that renders it possible to produce hyperemia in the tissues with radiant energy; and to a far greater depth than by the method of convective heat, as by applications to the surface of hot water bottles, poultices, or other means. Gilman Thompson demonstrated the limited effect of convective heat as applied by this method; and the author first called attention to the comparative effect of radiant light and heat upon the tissues in a previous work (2).

SOURCES OF RADIANT ENERGY

Natural Sources.—The sun is the great natural source of radiant light and heat and calls for practical consideration here. Other natural sources of light are the radiations from radium, uranium, and other radioactive bodies. In the treatment of this subject, however, the sun only will be considered.

As previously stated, there is objection to continued exposure to the sun's rays if the body is to receive special stimulation from the radiations for considerable time, except when passed through glass, as in solaria, when the ultra-violet rays are filtered out.

The action of the sun's rays upon air and water is prophylactic, rendering natural environment more healthful. A room where the sun's rays enter direct is far more healthful than a room which is lighted by reflected rays; ventilation not alone supplanting the beneficial effects of radiant light. The light, however, as previously stated, should be allowed to pass in for a time through the open window, and not only through the glass window panes.

The sun's radiations may be utilized for therapeutic purposes in places where it is impossible to obtain the electrical current; when, by passing the sun's rays through condensing lenses, it will be possible to increase the intensities for local treatments.

The *solarium sun bath,* or the bath before the closed window where the sun enters, allowing the sun to shine upon the nude body, is of great value in the treatment of anemic and atonic conditions, and can be arranged for in many homes by reflecting mirrors and otherwise, so that patients who are bedridden may receive the benefits of the stimulating influences of radiant energy under conditions in which artificial light cannot be provided.

At *sea bathing resorts,* where patients are exposed to the sun's rays, a large measure of benefit may be derived from the sun's rays as well as from the relaxation and the bathing. If persisted in too frequently and for too long exposures it becomes distinctly an over-stimulating measure. At some sanatoria provisions are made by which patients, male and female in separate enclosures, disrobe for several hours daily for exercise in the sun's rays, deriving undoubted benefit from such exercise in the open. Dr. Richard A. Nunn once said that, "When Patagonia was discovered the natives were largely unclothed and were a comparatively healthy race; but when civilization instituted clothing and houses in which to live, they died in large numbers of tuberculosis." The fact that human beings are so clothed as to shut out the light from the body undoubtedly accounts for the marked improvement that so many patients derive from the systematic applications of radiant energy, as by the light baths and the high candle-power lamps as employed at the present time.

Artificial Sources.—The artificial sources of radiant energy are the electric arc, Cooper Hewitt lamp, and the incandescent and tungsten lamps.

The Electric Arc.—The electric arc has been more or less employed since the first introduction of radiant light and heat in therapeutics. The radiations from this form of lamp are much richer in ultra-violet than the sunlight, particularly so when electrodes having iron cores are used in connection with the lamps. The benefits are those which may be shown to be derived from the presence of the combined frequencies, including the higher frequencies of the spectrum.

The *disadvantages of the arc light* are due: (1) To the objectionable effects of the higher frequencies previously mentioned; (2) to the fact that the light must be administered generally to the patient in the upright posture, or lying upon the side, because the flying particles of carbon will fall upon the patient if lying beneath the lamp; (3) to a negligible quantity, which may be considered however; the greater cost for current than for the requisite intensity of radiation from the incandescent or tungsten lights; (4) to the fact that when the arc light is administered to a patient in a closed bath it is impossible for some patients, and all patients under extreme conditions, to inhale and withstand the fumes from the gases thrown off from the arc lamps, composed, as they are, largely of nitrous acid and ozone, which are produced in large quantities by the

electric arc; (5) to the deleterious effects of prolonged exposures of radiant light from the arc light, except when a glass screen intervenes, due to the tanning of the skin, which finally interferes with the subsequent beneficial effects in cases in which it is desirable to continue for a considerable time the administration of radiant light and heat for increasing the conditions of nutrition and metabolism of the deeper tissues. These objections are only relative and can be, in a large measure, obviated by the use of colorless glass screens, and otherwise be made of practical utility. There are, however, methods more convenient and more practical.

The Incandescent Light.—The incandescent light as a source of radiant energy has come into very general use, and is destined in the future to fill a very important place in therapeutics. This form of lamp combines with the radiant light a very large percentage of radiant heat. The combined radiations are particularly valuable in inducing deep hyperemia, and in other ways improving the processes of metabolism. High candle-power lamps of this sort are always very convenient for applying the radiations. The lamps of larger sizes are suspended by a counterweight, and applied from directly over the patient while lying upon an operating table. The high candle-power lamps, applied with the patient lying down, can be brought nearer the body than the arc lamps and moved about, thereby employing a degree of intensity of heat that could not be borne when the light is fixed in one position. This enables the operator to administer the radiations with greater efficiency by employing a degree of energy that could not be borne if held in one position, shortening the time for administration, and, in addition, producing marked deep reflex effects upon the remote spinal centers, arousing them to greater functional activity.

The Tungsten Lamp.—The tungsten lamps, with which the luminous radiations are greatly accentuated by the fluorescence of thorium, which is incorporated in the construction of the filaments, produce a light of far greater intensity than the incandescent lamp, but with the same candle power have an emphatic deficiency in heat radiations. If these lamps are constructed, however, so that the heat radiations are all that can be tolerated by the patient when the lamp is suspended for operation at a practical distance, the added luminous effects appear to add a distinct advantage. If, however, these lights do not possess the requisite proportion of the lower frequencies to produce intense heat, their effects upon metabolism are far less beneficial than those of the incandescent lamps, which produce a large amount of heat. These lamps recently came upon the market and are now on trial.

Mercury Vapor Lamps.—The murcury vapor lamps of Cooper Hewitt have received some recognition from the profession, but have the same objectionable features as the arc light, in that they are rich in the higher frequencies. The radiations have also a very low percentage

of the lower frequencies, and, consequently, are inadequate in the amount of radiant heat projected. It cannot be too generally emphasized in this connection that radiant heat undoubtedly plays a most important part in the therapeutics of radiant energy, by the induction of hyperemia and elimination.

THE KROMAIER LAMP.—The Kromaier lamp is constructed in one particular as the Finsen and London Hospital lamps, i. e., they are provided with windows of rock crystal for transmitting the ultra-violet radiations. These lamps do not possess any special merit in therapeutics except for the treatment of certain local skin diseases where the irritating ultra-violet radiations may be indicated when they are generally effective. They are probably not superior in this respect to lamps made with iron electrodes or those of other composition for operation with the high potential current from high frequency apparatus. These lamps project radiations very rich in ultra-violet, and are provided with a window of rock-crystal.

APPARATUS

Various types of artificial lamps have been, from time to time, upon the market, keeping pace with and indicating the views and demands of the time and the stage of development of the therapeutics of radiant energy, respectively; some types being produced to meet advancing demands, and others becoming obsolete as methods change.

The Finsen Lamp.—The Finsen lamp, which at first employed the sunlight and later an arc lamp of intense candle power, which was energized in front of several tubes provided with rock crystal windows at the extreme end opposite the light, was arranged to treat four patients at one time, and was so employed in the Finsen laboratories and hospitals and institutions elsewhere. These lamps were very much in vogue at one time for the treatment of lupus vulgaris and lupus erythematosus. Other means have since given so much more prompt and equally as good if not better results that the methods and apparatus of Finsen are rapidly falling into disuse. Reference, however, is made to these lamps, because so much has previously been said of them in connection with the general topic of phototherapy, and because historically they led to the better recognition of light as a therapeutic measure. That they will be hereafter installed with therapeutic outfits is doubtful, because these lamps are now practically obsolete. The same is true of the London Hospital lamps and the types of the French investigators, Lortet and Genoud.

Marine Searchlight and Its Successors.—Before arc lamps of special construction for body administrations of radiant light were manufactured the modern marine searchlight was adapted by Cleaves to therapeutics. These high candle power arc lamps have been followed by the manufac-

ture of smaller lamps which are usually efficient, and consume far less current than the marine searchlight. By placing these smaller arc lamps nearer the patient they are quite as efficient as the marine searchlight of higher candle power, producing as great heat as can be tolerated over a considerable surface. This type of lamp as previously stated, however, is not of such practical value as the high candle power incandescent lamps which permit of the administration of radiant energy to the patient reclining, and which may be readily moved about.

High Candle Power Incandescent Lights.—The electric incandescent lamps of high and moderate candle power are destined to occupy a very important place in therapeutics. This type of lamp is now made by numerous manufacturers, and there is comparatively little difference in the features of the lamps as to their therapeutic value.

The writer prefers the larger lamps which are so provided with reflectors as to project beams of varying intensity, thereby permitting localization of the more intense beams upon the spots or areas where there is greater demand for local effects, as over painful or inflamed tissues. With lamps which throw a diffused light it is not possible to localize effects in this manner. Over small areas, where local infection is present, a 50 candle power lamp provided with a handle and cord, and attachment for any lamp socket, is quite as effective as the larger lamps, and it is always possible with these to localize the effects over the seat of pain and infection. A lamp of this type has been manufactured, which is provided with a stand supporting the lamp and a motor and a combination which gives the lamp a swinging motion. This lamp, being adjustable, is practical. When placed in position and adjusted, it does not require an attendant to make the prolonged applications so often necessary, as when treating otitis media.

Various types of construction of lamps of high candle power are now on the market. The tungsten lamp is one of the most practical lamps so far produced, the candle power being approximately 500, and when applied very close to the body seems to be rich enough in thermic rays to produce both superficial and deep hyperemia. When it is possible to combine these qualities, the additional volume of luminous rays seems to be a distinct advantage. If, however, the increased luminosity should prove to be at the sacrifice of the thermic rays, the luminous rays would not offset the effects of the heat rays which are incidental to the production of the deep hyperemia in the tissues.

The Minin Light.—The Minin light, devised by Prof. Minin of St. Petersburg, employs a bulb of 50 to 100 candle power of natural blue glass. The claim that this light produces an anesthetic effect has not been substantiated by the writer.

Colored Screens.—Variously colored screens have been made for use with the different sizes and types of therapeutic lamps, but the writer has

yet to find any special or striking benefit to be derived from these screens which filter out some of the spectral rays.

Göerl Lamps.—In accord with a well recognized fact, that the spark of an electric arc, or between oppositely charged capacities, is rich in the higher frequencies, has led to the manufacture of various iron electrode and other arc lights, which have been used on the principle of the Finsen method of treating superficial infections. Some of these lamps are of the so-called Göerl type, and are made with two to four small balls so arranged that sparks will pass in the circuit before a reflecting surface, projecting a light rich in ultra-violet and the higher frequencies, the volume depending on the amperage of the current passing.

Light Bath Cabinets.—Light bath cabinets are an important addition to the armamentarium of hospitals, sanatoriums, and offices provided with the means of properly caring for patients for whom they are indicated. The writer is convinced that for hospital, sanatorium, and office use the reclining bath is generally to be preferred to the upright bath, as feeble patients when fatigued are liable to attacks of syncope when seated for twenty minutes to one half hour in an upright position.

It has been suggested by Dr. E. C. Titus that the light bath should be ventilated, permitting the air to pass up through and out about the patient. While this may be of advantage in some cases, in most instances the writer believes that the accumulating heat in the light bath, together with the radiant energy applied, effects at least more energetic diaphoresis than when ventilated. The emanations being actively excreted from the skin during the process, it is practically impossible for any deleterious materials to be absorbed by the skin of the patient, whereas in passing upward with the evaporation they will be inhaled by the patient when ventilated as suggested, if precautions are not taken.

The incandescent bulbs in the light bath should be so arranged that they are over and about the patient if reclining upon a couch in the bath. There should be at least 50 or 60 lamps in the ordinary cabinet, and the lights should be so placed that they will be at a convenient distance—approximately 18 inches—from the patient, or as near as possible without bringing the points of the incandescent bulbs too close to the body of an obese patient. If the tungsten lamps are employed in the light bath instead of the ordinary carbon filament lamp, there will be a greater luminosity, but the number of lights will necessarily have to be increased to nearly twice the number, in order to maintain a temperature approximating 200° F. in the bath. There is no doubt but that the luminous effects of these lights will add much to the therapeutic value of the radiant light bath.

Mirrors and reflecting surfaces within the light bath are of so little, if of any, practical value that they are not to be considered. It is not even necessary that the asbestos be painted with an enamel paint to give the sur-

face a glossy finish, as it has been shown that light is reflected as largely from a dull white surface as from a glazed surface. In the arrangement of switches in connection with the rows of lights in the bath, it is practical to have the bath so wired as to be able to throw on alternate rows of lights, in order that when the light is partly turned off the luminosity may be equally distributed to the surface of the patient.

Numerous cabinets have been constructed in which the *arc light* has been employed either alone or in connection with incandescent lamps. Care must be taken that patients are not exposed for too long a time in these baths, lest the skin become seriously blistered. There is very little, if any, advantage with this type of lamp, either alone or in combination, for reasons previously stated.

PHYSIOLOGICAL EFFECTS

With the advance of knowledge in the employment of physical agents in therapeutics, we come nearer to an exact knowledge of the effects and indications which afford a rational basis for their administration in therapeutics. In light therapy, as elsewhere, the better understanding of the physical properties of radiant light and heat as applied to the human body has given us much upon which to base a rational understanding of the physiological effects.

As has been previously stated, radiant energy from luminous sources penetrates for considerable depths into the body, with the production of distinctly well-defined physical effects due to the transmission of vibratory energy and secondarily influencing the chemical processes by their effects upon the nutrition and the nervous mechanism of metabolism with increase of the functional activities.

Radiant energy from the numerous sources as it passes through the parts produces a varying degree of heat in the tissues depending upon the intensity and other characteristics of the radiations. The associated lower frequencies of the infra-red are especially penetrating and energetic in this particular. The luminous and infra-red radiations present a marked contrast to the Roentgen ray and the ultra-violet radiations, neither of which produce perceptible heat, whereas the former are energetic in heat effects. As the tissues become heated by impinging radiant energy, the effect is not only local, but also general, the blood, which becomes heated in passing through the heated tissues, conveying the warmth throughout the body, produces a general glow with perspiration. When such applications are prolonged the secretory and excretory functions of the body are all quickened, as is evidenced by the increased activity of the sweat glands. The perspiration evaporates, producing a cooling at the surface, thereby maintaining an equilibrium of temperature throughout the organism by the cooling effect derived from absorption by the latent heat of evaporation.

In this manner the administrations of radiant energy produce a complex influence upon metabolism by quickening the process of elimination of waste products from the organism, and maintaining a uniform body temperature.

Effects upon Metabolism.—The influences upon metabolism cannot be attributed alone to the effects of heat; for the luminous rays act also directly upon the blood cells present in the circulating blood stream, the effect becoming more general as the tissues irradiated become hyperemic under prolonged exposure. In this manner, in a short time, the volume of blood in the body has been generally all exposed to the oxidizing and sterilizing influences of light.

In the administration of radiant heat, therefore, the effects cannot be considered as distinctly local, they being transmitted through the circulation to all parts of the organism. The quickened activity of circulation and the beneficial effects of light upon the blood stream still further accelerate the functional activities. It is also shown practically that under daily administrations of light in anemic subjects there is a gradual increase in the hemoglobin, as well as of the percentage of red blood corpuscles. In noted instances the red blood cell count has thus been increased fully 1,000,000 in thirty days.

Local Effects.—The local effects of radiant light and heat from the usual sources are derived from the combined actions, luminous and thermic, of the radiations, in which they far exceed other means. Except, possibly, when, by the employment locally of extremely high temperatures by convective dry heat, as when an arm is rendered hyperemic by temperatures of 400 to 450° F. under proper conditions for the treatment of local septic infection in the management of which the latter method is uniformly successful in the hands of those who are familiar with the method of employing it.

The induction of hyperemia, as previously stated, is attributable to local stimulation, when heat is applied, by inducing an effort of the vasomotor mechanism to maintain an equilibrium of temperature. Hyperemia when induced by the applications of heat, radiant or otherwise, produces in the tissues so vascularized three distinct effects associated with the increased flux of blood into the tissues. (1) There is an increased metabolism associated with the transmitted cardiac impulse, which arouses the tissues to greater cellular activity; (2) there is increased nutrition present with the increased blood supply; and (3) there is a relative increase in the number of phagocytes in the tissues with the increased flux of blood through them.

When hyperemia is induced by the administration of cold the chilling of the tissues does not favor the active processes of metabolism, and likewise renders the phagocytes inert; hyperemia does occur, however, in all subjects except those in whom the resistance is much below normal.

When infection is present in the tissues irradiated the intense radiations of light and heat have a depressing influence upon the forms of life that are walled in within the infected tissues, while the circulating blood passes rapidly through the tissues relaxed by the heat, in its efforts to maintain the equilibrium of temperature. At the close of a prolonged administration of radiant light to an infected area when the tissues are relaxed, the conditions are favorable for an active process of phagocytosis, the germs having been stunned by prolonged exposure to the irradiations, and the blood being still present in relatively large quantities. Clinical experience in this connection justifies the assumption that when radiant energy is applied it is particularly favorable for active phagocytosis, and coincidently unfavorable for the propagation and existence of germ life.

The antiseptic action of the higher frequencies was shown by Neils Finsen when he demonstrated the active effect of the ultra-violet radiations in destroying germ life as in the air and water—when the germs were destroyed in the tissues rendered anemic. It is probable, in addition to the effects sought by Neils Finsen—the reaction—which was always sought in the treatment of lupus by his method, that the hyperemia induced had very much to do with the recovery of the patients; because there were an increase in phagocytes and a clearing out from the tissues of the inert germs and the other waste products of metabolism.

Summary.—It must be conceded that in the treatment of local and constitutional conditions the radiant light and heat radiation administered does induce marked effects. These have been summarized as follows in the author's work on "The Therapeutics of Radiant Light and Heat and Convective Heat":

"I. *The effects upon metabolism,* local and general, are due to (1) the induction of increased local activity of elimination and tissue building; (2) diffusion of heat throughout the body through the channels of circulation; (3) the increased general elimination by the perspiration which is induced by the general diffusion of heat, when exposures are extensive and prolonged; (4) increased oxidation, from heating of the tissues, and the local action of radiant light upon the blood in the dilated capillaries; and (5) the effects upon the remote spinal centers due to peripheral stimulation of the end neurons by heat and light radiations.

"II. *The effects upon simple inflammation,* unaccompanied by infection, are (1) to induce general tissue relaxation, with relief from pressure and pain; (2) to increase local metabolism and elimination, relieving tissues from the irritating products of defective metabolism as present in conditions associated with myalgias, infectious arthritis, eczema, and similar conditions; and (3) in conditions of mild traumatic injury, treated promptly after injury, to remove or prevent early stasis and cure the condition. It is, however, ineffective after stasis when induration is once fully established.

"III. *In acute and sub-acute infectious conditions alone,* or in connection with other measures, it inhibits germ processes or increases local hyperemia or both. (1) It increases local hyperemia in the region of infection with a relative increase of phagocytosis. (2) It inhibits the activity of the germs through the intensity of the radiant light and heat radiations. (3) It stimulates the elimination of toxic materials, local and diffused, by the induction of active perspiration and also increases, through other channels, general tissue oxidation.

"By these means local phagocytosis is stimulated, the germs inhibited and devoured, and the toxic materials eliminated.

"IV. *Derivative effects* are induced when extensive exposures are made, rendering the surface hyperemic by prolonged applications of high candle power incandescent lamps over front, back, and sides, or by the arc or incandescent light bath and by the coincident profuse perspiration induced; (1) lessening the quantity of blood in remote congested regions and in the larger arteries and veins; (2) lowering arterial tension; and (3) coincidently promoting extensive elimination of the locked up effete matter resulting from poor metabolism."

It will be readily appreciated from the foregoing that the therapeutic scope of radiant energy is such as to fill a wide range of therapeutic indication.

Antagonism of Radiant Light and Heat and the Roentgen Ray

Another effect, not essentially a therapeutic effect, but one in which the therapeutic application is indicated in connection with the employment of another therapeutic measure, the Roentgen ray, deserves mention in this connection. More than seven years ago the writer, while employing the Roentgen ray and light experimentally to the same tissues on the same day, with a view to the possibility of diminishing what was then deemed the deleterious effects of the Roentgen ray, found that when the two were administered at the same sitting the effects of the Roentgen ray were practically neutralized, and little or no beneficial effects were derived from the conjoint application. This suggested the probability that the effects of the two forms of radiant energy were diametrically opposed to each other. And so it has since been demonstrated both in the author's experience, and the practical experiments of Dr. Edward C. Titus. He demonstrated not only on the sterilizing influences of the X-ray upon the seeds of plants, but also the counter effects of radiant light and heat upon seeds and eggs that had been irradiated. When they were subsequently exposed to radiant light and heat it was found that the fertility had been restored. This discovery has given this form of energy a very important field in radiography and radiotherapy; for in all cases in which a dermatitis appears, if taken early, the employment of radiant light and heat

with an energy relative to the demands induces an increased influx of arterial blood throughout the affected tissues, and at the same time increases the activity of local tissue metabolism, promptly restoring vitality to the parts. This is the effect in all cases when applied before necrosis is actually present. This counter action of radiant light and heat has removed all misgivings as to the dangers of X-ray applications when employed intelligently.

THE INDICATIONS

The indications for the use of radiant energy in therapeutics, as may be inferred from the foregoing observations, include a fertile field in therapeutics. Success from its employment, however, depends upon strict observance of technique, particularly as to duration and intensity of administration. The methods of employing radiant light and heat must be directed to the production of definite physical effects if satisfactory results are to be obtained. It will be the writer's endeavor, therefore, as far as possible, to outline indications and methods of administration.

THERAPEUTICS OF RADIANT LIGHT AND HEAT

In considering the therapeutics of radiant energy, a classification will be followed, which recognizes conditions with relation to causes and the effects sought.

Inflammation may be considered of two distinct types—that arising from infection, and conditions arising from other causes, as mechanical or chemical injuries, and defective metabolism.

Infectious Type of Inflammation

The infectious type of inflammation is manifested in two ways, as arising directly from a germ process generally localized, and from toxemia, which may have its origin in some remote infection.

It is difficult to say that radiant energy is not specifically advantageous in the treatment of all types of infection. There has not, however, to the present time, been sufficient clinical experience to demonstrate its value in all infectious diseases associated with marked constitutional symptoms, as in typhoid fever and pneumonia. There is no contraindication for its employment in these cases, and the possibility of affecting localized germ processes as present in infectious fevers promises much from the same point of view as in the treatment of other localized infections.

Localized Infections

In tuberculous, streptococcic, staphylococcic, and gonococcic infections the therapeutic employment of radiant light and heat undoubtedly plays an important part, particularly so in the ***streptococcic and staphylococcic*** processes, which are the most common, and, when uncontrolled, of the most serious types of infection.

In the writer's experience no recent investigation has given greater satisfaction than that concerned with the treatment of local and general infection.

The *effects of radiant light and heat* in the treatment of local infection have remarkable possibilities, increasing as it does the activities of the normal defences, while at the same time depressing the vitality of the germs exposed. The work of Neils Finsen in treating the two types of lupus was the first to arouse an interest in photography and its possibilities for destroying germ life.

Finsen's efforts were directed to the employment of the higher frequencies of radiant energy, on account of the well-known sterilizing properties, particularly of the ultra-violet radiations. In this he succeeded by the methods previously described. When, however, he sought to obtain a reaction, a thing he always advocated, the increased local tissue hyperemia introduced a factor involving another important principle. He gave no significance, however, to the fact that such hyperemia increased the number of phagocytes at the site of infection, which certainly did contribute another factor to the local destruction of the germs.

From clinical results it seems to be fully demonstrated that the multiplication of phagocytes in the tissues plays an important part in the removal of the local infection, and otherwise favors the restoration of the diseased tissue by increasing local nutrition and metabolism. For the part played by hyperemia in the treatment of infection, as previously stated, is threefold. (1) It increases the nutrition in the tissue; (2) it increases the metabolism with increase of tissue oxidation; and (3) it increases in numbers the presence of phagocytes under conditions favorable to a positive chemotaxis.

The writer has demonstrated, clinically, the principles of hyperemia and has constantly verified its practicability in the treatment of particular types of local infection.

The method described by various writers as "Bier's method" has for its intent the empiric induction of hyperemia; whereas, if the method has succeeded, it has been due to increased presence and activity of the phagocytes under conditions of hyperemia. That this is what does take place is well demonstrated in the results obtained with the method

of employing dry hot air in the treatment of local infection. Uniform success is obtained when temperatures of 350 to 450° F. are employed with the parts carefully wrapped in Turkish toweling, continued for 30 to 40 minutes once or twice daily. The local temperature, when this method is employed, is never sufficient to destroy the germs, because the rapid flux of blood maintains a safe temperature, hence the destruction which certainly *does* take place must be due to the activity of the phagocytes.

Radiant light and heat, when employed in the treatment of local infection, should aim always to produce, by prolonged application, intense local hyperemia for the purpose of flooding the infected tissue with an abundance of fresh blood. In cases of acute or chronic infection it is possible by this means to destroy the local infection in the former, leaving the tissues in a normal condition, and the latter with changes relative to the hyperplasia or necrosis, which had preceded the administration. This condition occurs often in carbuncles or other large abscesses that are not arrested in the earlier stages.

Abscesses.—An effective method of treating abscesses is to precede the employment of radiant light and heat with X-rays, employing what would approximate a massive Saboraud dose or the approximate equivalent of thirty or forty minutes' exposure with an average dose or intensity ordinarily used on alternate days for the treatment of epithelioma. This is followed after twenty-four hours by the systematic employment twice daily of prolonged local applications of radiant light and heat as near to the surface as they can be comfortably borne by the patient without compromising an active hyperemic effect. These treatments should be continued for at least one half hour, and will, as a rule, result in the abortion of the process within thirty-six to forty-eight hours. When, however, an abscess is far advanced, evacuation should precede the administration of radiant energy, when, if tissue necrosis has not intervened, the recovery will generally be prompt and satisfactory.

Acute Otitis Media.—Acute otitis media, treated by this method, may be uniformly aborted if the treatment is instituted as soon as the earache is causing severe pain, before pus has formed, and is often effective in advanced cases, if sufficient thoroughness is employed in the application. In these cases the rule should be to apply radiant light and heat, for convenience, with a small lamp of 50 candle power until the pain has subsided, repeating the application upon the recurrence of pain. As these small reflecting lamps can be used in so many houses at the present time, the family or nurse in charge should be directed to keep up a pretty steady application of radiant light and heat from the onset of the pain in the ear. Otitis media is usually caused by a pharyngeal complication. The coincident treatment of a local pharyngitis is necessary to prevent recurrence.

Chronic Otitis Media.—In suppurative otitis media chronica, when not of long standing, in which the ossicles are not necrotic, the condition is promptly cured in most cases by daily applications of radiant light and heat for periods of at least one half hour to one hour daily, and in severe cases two daily applications may be advisable. It is possible to cure most cases in from two to three weeks, and often within one week; thus effecting a complete recovery from a condition which will often have been present for months. If cases of acute and subacute otitis media are treated systematically with radiant light and heat before mastoiditis intervenes, there will be but rare occurrence of that condition.

Mastoiditis.—Mastoiditis, in the early stage, or cases in which the process has not been active enough to have resulted in necrosis, the affection may often be aborted and cured by the systematic use of radiant light and heat. The relief from pain and prompt fall of temperature will be the indication that the local pyogenic process is in abeyance. That the possibility of these results is not recognized by aurists generally is often unfortunate for the sufferer. The method is so unobjectionable that the only argument that the surgeon could advance against its employment would be the danger of delay. The treatment should be instituted as early as possible and pending an operation in all cases, and also following operation if one is demanded by the conditions. It will be shown in the following suggestions that radiant light and heat may wisely be used in the treatment of all accessible post-operative conditions.

The writer has himself verified the success of this method in the treatment of two cases of mastoiditis and numerous cases of otitis media.

The first reports of the success of this mode of treating otitis media and mastoiditis must be credited to Dr. Herbert F. Pitcher (1), who reported successful results in a number of cases. These results have since been duplicated by numerous observers who have employed them intelligently, and mark a distinct advance in the management of these distressing affections.

Suppuration of the Frontal Sinuses.—This condition may be treated successfully in the same manner. In these cases the treatment should be employed at least once daily for a long time. The following case well illustrates the method and result:

Miss S., age 35, a patient who had been a subject of pulmonary tuberculosis, was referred to the writer on December 15th, 1910. She complained of having had a profuse discharge from the nose which had suddenly ceased, when she had begun to suffer from intense pain and discomfort in the region of both frontal sinuses. A small, 50 candle power incandescent lamp with parabolic reflector was used in the treatment. The patient was instructed to apply it herself, passing the reflecting lamp back and forth for one hour daily over the forehead. The application was made with the elbows resting upon a table with the reflector so directed

that the greatest intensity of the radiations fell directly upon the sinuses.

After three applications a thick mucopurulent discharge was re-established. The treatment was continued daily for one month. The discharge became gradually less thick and purulent, and then serous, and within the month entirely ceased. The pain was relieved soon after the first purulent discharge was established. This patient has had no recurrence whatever of the affection during the past nine months. This case represents a fairly typical one of the sort, and forecasts that similar results will be obtained in most cases; because this patient, owing to an unfavorable general condition, was below the average resistance.

Antral Disease.—In disease of the antrum, in the early stage before pus has accumulated, undoubtedly the same method will be successful. It is readily demonstrated that light shines out through the antrum when a small electric lamp is placed in the mouth. There is no reason to doubt, therefore, that the application of radiant light over the same region as in the preceding cases from without should produce the characteristic effects of radiant light and heat upon local infection within the antrum. In advanced cases, after the pus has been drained through an opening made by drilling or extracting a tooth or both, from the floor of the antrum, this method should be thoroughly effective and promptly result in complete recovery as in the frontal sinuses and otitis media cases.

Tuberculous Infection.—In the treatment of local tuberculous infection light is a very valuable accessory to the thermic effects of direct d'Arsonvalization, and Roentgen ray applications. The effect of radiant energy upon germ life in tuberculosis, as previously shown in other cases, is to produce marked depression upon the germs while coincidently increasing local phagocytosis and tissue resistance.

In *tuberculous adenitis* a large percentage of the incipient cases would require no further treatment than systematic applications of radiant light and heat. In these cases the results are uniformly successful, except when suppuration has intervened, when the process of recovery will, as a rule, be very tedious. Radiant light and heat, however, following the systematic use of the Roentgen ray, is one of the most valuable adjuncts in the treatment of these cases.

In *tuberculous arthritis* the hyperemia induced by radiant light and heat, as in other conditions, lends great assistance to the Roentgen ray and thermic effects of the direct d'Arsonval current, with the possibility of relieving the joint in early cases.

In *tuberculous peritonitis,* following systematic X-ray treatment, the employment of radiant light and heat is often effective in restoring the parts to normal. In all cases in which the X-ray has been used for a considerable time, subsequent applications of radiant light and heat are often capable of restoring the underlying tissues to a normal condition when the inhibitory effect of the ray has lessened the tissue vitality. This

is particularly important in tuberculous subjects, in whom lowering of tissue resistance is fraught with danger of local recurrence.

Intestinal Infection.—In intestinal infection, or conditions of fecal putrefaction, with impaired secretion, prolonged applications of radiant light and heat are remarkably efficient, in connection with diet regulation and systematic evacuation, in correcting various irregularities in the intentinal flora, both by increasing the normal tissue resistance and secretion and by retarding the processes of germ development. Applications, to be effective in these cases, should be made for from 20 to 30 minutes daily over the abdomen with a high candle power incandescent lamp moved rapidly about.

Pelvic Congestions.—In various pelvic congestions, associated with or without infection, the application of radiant light and heat not only gives great temporary relief from pain, but, at the same time, facilitates, in many cases, a cure of the local condition, when employed in conjunction with other indicated methods of treatment. Radiant light and heat should never be used during daily administrations of the Roentgen ray, but following series of applications, when a dermatitis may have appeared, or from the restitution of the tissues, following long series of X-ray radiations.

Appendicitis.—In appendicitis the suggestion of treatment with radiant energy presumes with audacity on the present conceded precinct of surgery. This measure, however, seems to be indicated instead of ice or convective heat in mild cases and in all early cases of appendicitis. The writer's experience in three cases in his own family, who were under the close observation of a surgeon from the beginning of treatment, during the past year resulted in a complete relief of each with the application of no other measure than radiant light and heat. In one case, in a young woman twenty-one years of age, after an acute appendicitis, the first twenty-four hours having begun with severe pain, treatment with radiant light and heat was instituted before Dr. Herman Grad, the surgeon, reached the house. Administrations of radiant light and heat were given for periods of one-half hour with a high candle power lamp. During the following twelve hours the temperature was reduced from 101½° to 99° F., and there was complete relief from pain, except on pressure, and the local muscular tension was markedly diminished. The treatment was persisted in for three days, when it was discontinued, the symptoms having completely disappeared. For one year there has been no sign or symptom of recurrence.

Another case was brought to the city after three days of suffering, during which ice had been applied constantly over the appendix. The patient, a boy seven years of age, arrived in town late in the evening, and radiant light and heat from a high candle power lamp was applied almost constantly during the night, when, by morning, the temperature

had fallen from 102° to 100° F. The surgeon who was called in attendance advised the continuance of radiant light and heat for another day, when the pain had gradually ceased and the temperature had fallen to 99½° F., and the muscular tension was much less marked. The applications were continued in this case, under the observation of the surgeon, for two weeks, when the child had completely recovered, and the appendix, which, when he came under observation, was much enlarged and indurated and could be easily palpated through the abdominal wall, could not be readily made out by palpation, nor pain induced on deep pressure.

These cases are referred to as suggesting the possibility of arresting cases of catarrhal appendicitis in the early stages. The writer here pleads guilty of infringing upon the accepted rules, but under the observation of prudent and competent surgeons. The results leave no feelings of compunction, but, on the contrary, would dispose the writer to repeat the same method early in every case, and in all cases who refuse an operation.

In *chronic appendicitis* radiant light and heat as an adjunct to the Roentgen ray and the direct d'Arsonval current has often been effective in checking the process and relieving the patient from all local pain and discomfort. Adhesions in these cases seem to be the only condition that precludes the possibility of complete recovery from the local symptoms, when, if the alimentary canal is subsequently kept in a proper sanitary condition, there is not much liability of the trouble recurring.

Erysipelas.—Erysipelas, when treated by long applications of radiant light, has given remarkable results in the few cases in which it has been observed by the writer. There is probably nothing that promises greater relief from the discomfort arising from the conditions associated with erysipelas, with the possibility, also, of limiting the process, than the local applications of radiant light and heat. The relief has been prompt and the lesions have disappeared within forty-eight hours in the cases observed.

From the foregoing observations, the writer would recommend a more general investigation and institution of radiant light and heat in the treatment of infectious conditions. It will be found that, when systematically employed, the possibilities are remarkable, from the action of radiant light and heat in infectious processes.

Inflammation Arising from Toxemia

Toxic inflammation, as affecting the heart, joints, throat, and other parts of the organism, is usually of intestinal origin, associated, in most cases, with the presence of unusual proportions of gram-positive and other offensive bacilli in the intestinal tract. Indications in these cases may be, first of all, intestinal sterilization, which includes thorough evacuation. Radiant light and heat plays a very important part in the management of these cases.

Radiant light and heat baths are particularly effective in forcing the elimination of systemic poisons with the perspiration, and, at the same time, by quickening the general metabolism and improvng nutritive processes, thereby increasing the resistance against the toxic invasion. The application of radiant light and heat with a high candle power incandescent lamp over the abdomen is remarkably effective in improving nutrition, and also in impairing the activity of the intestinal bacteria.

Cardiac Toxemia.—In toxemia affecting the cardia there is probably no agent which contributes more to the relief of the local condition than the intense local application of radiant light and heat, except, possibly, the removal of the cause, as the source of the toxemia.

Joint Conditions.—To inflamed and painful joints, the seat of toxic disturbance, the prolonged applications of radiant light afford remarkable relief to sufferers from so-called rheumatism, rheumatoid arthritis, and other local toxic inflammations. The cure of these conditions, however, looks to the rational treatment of the *symptom-complex.*

Parenchymatous Nephritis.—In parenchymatous nephritis, which may or may not be of toxic origin, the radiant light bath is one of the most valuable measures for the relief of the condition, removing, as it does, through the sweat glands, much of the toxic material and the nitrogenous waste which should properly be eliminated by the kidneys; and, at the same time, the general metabolism of the patient is materially increased.

Inflammation not Associated with Infection or Toxemia

Simple Inflammatory Infections.—In simple inflammatory affections, or those arising from mechanical injury or impaired metabolism, the conditions are often greatly relieved by radiant light and heat, but not so effectively as those arising from infection, because, in most cases, there is an associated infiltration or induration which is more effectively removed by the static current. The application of radiant light and heat does not relieve local induration. The pain in neuritis may be lessened by the application of radiant light and heat and in other conditions where induration is present. This is due to the softening by relaxation of the hardened tissue, relieving the pressure upon the nerve filaments, and not to dissipation of the induration. Light and heat, thus applied, relieve pain but temporarily, it returning after a short period of rest. In the treatment of inflammation of this type, therefore, the influence of radiant light is that of an adjunct agent; and, when employed with the static current in the treatment of any of the conditions in which it is used, should always precede the static current.

Impaired Metabolism.—In conditions of impaired metabolism, where, for any reason, the functions of the organism are inactive or relatively inert, the administrations of radiant light and heat are particularly effi-

cient in stimulating local inactivities. This is especially the case in neurasthenic patients who for a long time have suffered from chronic constipation and relaxed conditions, and those in feeble health. In these, administrations of radiant light and heat, particularly to the trunk, are followed by marked improvement after weeks of treatment. With the restoration of active perspiration, which is, as a rule, deficient in these cases, as well as of the other secretions, the appetite improves, and there is marked improvement in the general health. In all cases the applications at each treatment should be made until the surface is distinctly hyperemic. The high candle power lamp should be swung very close to the patient and moved very rapidly, and, if he complains of too great heat, an occasional rapid movement of the hand over and against the surface at the places where the heat is greatest assists the patient to tolerate the intense radiations. Administered in this way, local hyperemia may be induced very rapidly. In very obese patients the applications should be made to the front, sides, and back; but ordinarily the applications to the front and back of the trunk are sufficient.

In *anemic patients* it is quite remarkable how promptly the percentage of hemoglobin and the red blood count increase when other conditions which have caused the anemia are coincidently treated, the light having a remarkably beneficial effect in this particular.

The *light bath* in defective metabolism, as associated with *nephritis, rheumatoid arthritis, gouty and other arthritic conditions,* is very beneficial, and the best means of eliminating toxic materials from the system, as it coincidently improves the general and local metabolism. The patient should receive this treatment on alternate days at least. The temperature of the bath should be raised rapidly to from 200° to 250° F., and the period of the bath should be from 20 to 30 minutes, according to the vigor of the patient, a rise of the patient's temperature above 100° F., or rapid acceleration of the pulse being an indication to cut off part of the lights, or discontinue the bath. These patients may be thoroughly rubbed and dried off after the bath, or, when a profound diaphoresis is desired, they may be wrapped up in a sheet or flannel blanket and allowed to rest for a considerable time. The rest may be followed by a tepid shower, or the skin may be dried and followed by a thorough massage, preferably with the vibrator. Another method is to submerge the patient when taken from the bath in a water bath at a temperature of about 100° F., and then gradually cool the water to about 70° to 80° F. by allowing a small stream to flow into the tub. The patient may then be thoroughly dried with towels and allowed to rest for a time. A long rest following a light bath is often of great benefit to feeble patients. When these baths are given frequently, as they may be in hospitals and sanatoria, the patients after the bath should be put to bed in a quiet place where they can rest, because a refreshing sleep will generally follow such

bath. When the light bath is installed, as it will be generally in sanatoria, this method of treatment will afford great relief in most feverish conditions, the fever being often due to the toxic poisons, which are largely eliminated in the radiant light and heat bath. The effect will be not only to reduce the patient's temperature by the evaporation of the perspiration, but also to relieve the patient from the toxic accumulations, which, as previously stated, may be largely the cause of the fever condition.

THE POST-OPERATIVE USES OF RADIANT LIGHT AND HEAT

The use of radiant light and heat following operations has not, to the present time, been adopted as it is certain to be when the degree of relief afforded by its application has been clinically demonstrated to the surgical staffs in the hospitals. Its employment is not only indicated for the immediate relief of the patient following an operation, but also to prevent the conditions of infection with induration in the margin of the wound, which often intervenes and delays union by first intention. Post-operative conditions of tenderness immediately following the manipulation of the tissues beneath the surface often result in the establishment of a degree of infiltration throughout the tissues evidenced by tenderness and swelling, which also retards the reparative processes. In other words, the tenderness following operation is due to local congestions, which may result in local stasis within the tissues immediately surrounding the site of operation. If, directly following an operation, prolonged application is made of radiant light and heat to the extent of inducing a diffused hyperemia throughout the tissues, the flow of blood throughout the tissues, if the drainage has not been too severe, will, if kept up for a half hour or longer, maintain the circulation and thereby prevent the establishment, as previously stated, of infiltration and stasis. This is manifested by the great relief from pain and tenderness that is afforded the patient when radiant light and heat are applied with thoroughness in this manner. If the patient is wheeled from the operating room to a room where light is applied over the site of the wound immediately after an operation, for half an hour, and through the thin gauze dressings, the best results are obtained. Following such applications the patient will relapse into a quiet sleep. The immediate relief from the pains of the operation and the tenderness following an operation is remarkable when this routine is carried out. If light is applied in this manner each time the dressings are changed, or twice daily through the dressings, it is remarkable how rapidly complete union takes place, and in how few cases there will be delayed union. The hyperemia induced not only increases the local nutrition, but, with the increased presence of phagocytes in the tissues, the likelihood of the site of the wound becoming infected is reduced to a minimum. This has been dem-

onstrated to the writer's satisfaction, and warrants, he believes, its careful investigation in private and hospital practice.

Treatment of Phlebitis

It is remarkable how much comfort can be afforded from the application of radiant light and heat in cases of phlebitis. The applications should be made for a long time, until the tissues are fairly hyperemic, when, to obtain the most prompt results, they should be followed by systematic applications of the static brush-discharge, until the tissues are softened by the removal of the local infiltration. This method is uniformly successful in all cases in which tenderness is still present; that is, in all cases except where the vein has become occluded. The writer has relieved cases in which the inflammation has been present for three to five months; in one of the cases of three months' standing, the saphenous vein was involved.

Radiant Light and Heat in Dermatology.

Radiant light and heat are indicated in the treatment of local skin conditions requiring stimulation, as in atonic conditions associated with infiltration and impaired metabolism. In such cases, the persistent induction of hyperemia is remarkably effective in restoring nutrition and promoting a restoration of the skin to the normal. This is true either when employed alone or as an adjunct of electrical treatment.

Eczema.—In cases of chronic eczema it is indicated, but contraindicated in cases of acute moist eczema. Desloges has reported a case of eczema of eight years' standing, covering the body, in which high frequency currents were applied to the hands for three weeks with complete success. To the eruption still remaining on the legs and surface of the body, however, the high candle-power incandescent lamp was applied. Under this treatment the redness gradually disappeared, the scars separated, leaving the skin in a normal condition after three weeks. The applications were made for twenty minutes, morning and evening. In this case, after two years, there had been no recurrence.

Psoriasis.—In psoriasis very favorable reports have been given of success by the use of the high candle power incandescent lamp. One writer reports over thirty cases in which he obtained remarkable success by the employment of this means. He reports that often no improvement was shown until after twenty or thirty daily applications; and that the treatments extended over long periods of time. In his experience the patches of psoriasis cleared up first in the center, became more pink, and then faded away.

Itching Erythemas.—In the itching erythemas the prolonged applications of radiant light and heat are often remarkably effective in relieving the disagreeable symptoms. These cases, however, require, at the same time, attention to the systemic cause of the eruption.

Acne.—In acne the stimulating effects of light in many cases assists in effecting the relief of the condition. In acne, however, there are usually better means of treatment.

Urticaria.—In urticaria, even in cases which have persisted for a long time, the result of long applications with radiant light is remarkably good. The writer knows of nothing that offers such prompt relief in these cases as long applications of radiant light and heat. In one instance, a case which had persisted for weeks was entirely relieved with one treatment to the whole body, which was made for fully one and one-half hours.

Varicose Ulcers.—In varicose ulcers the use of radiant light and heat daily with fairly long exposures is effective in promoting healing. When used alone it is often successful, but the result is not nearly so prompt as when employed in connection with the static brush-discharge, as in phlebitis; the application of the static brush discharge removing the infiltration.

The scope of indication for the employment of radiant light and heat, it will be observed, is large; and, though the writer in this treatise has but briefly touched upon the subject, it is hoped that what he has written will lead to more thorough investigation.

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CHAPTER X

RADIUM THERAPY

William Henry Beaufort Aikins

RADIOACTIVITY AND RADIOACTIVE SUBSTANCES

The property of radioactivity was discovered by Prof. Henri Becquerel of Paris in 1896, while conducting a series of investigations on the phosphorescence of uranium salts. He discovered that not only were spontaneous radiations emitted by phosphorescent uranic salts, but that they were also produced by salts of uranium oxid and protoxid and by the metal uranium itself, none of which were phosphorescent. From this it was concluded that the property of emitting a penetrating radiation belonged to the element uranium itself, quite apart from any of its chemical combinations. To this phenomenon the term "Becquerel rays" was applied.

In 1898 Prof. and Mme. Curie and M. Schmidt independently discovered similar rays in thorium, and, continuing her investigations into the radioactivities of various uranium compounds, Mme. Curie made a wonderful discovery. Uranium is found chiefly in the form of a black oxid from the mineral pitchblende. This is mined principally at Joachimsthal, in Bohemia, and, on comparing the radioactivity of this substance with other uranium salts, it was discovered that the pitchblende was three or four times more active than uranium itself. The only explanation for this was that some substance far more radioactive than any known element must be present in the pitchblende from Joachimsthal. Mme. Curie proceeded with the difficult task of isolating this element, and, after a series of prolonged and exacting researches, succeeded in extracting two substances. One of them was exceedingly active and was called radium, the other, which was much weaker, was called polonium, after Mme. Curie's native land, Poland. This was in 1900, and in the same year another new radioactive body was discovered by M. Debierne and called actinium. In 1904 a substance, radiothorium, was discovered by Ramsay and Hahn.

At present these are the chief radioactive bodies known, and, of these,

radium has aroused the most interest, not only to the physicist, but to the therapeutist.

Recently the salts of thorium have also been used in treatment, but, as their action can only be regarded as that of radium in a much less degree, we will confine ourselves to the use of this latter substance in the treatment of various diseases.

At the outset it must be conceded that the greater part of our knowledge of this agent, its physical and therapeutic properties, has been derived from the French school. To M. and Mme. Curie is due the honor of having isolated the substance and determined its physics and chemistry, while to Prof. Louis Wickham, of Paris, and his colleague, Dr. Degrais, belongs the credit of having brought to bear all the resources of science in order to put radium therapy on a sound and sure scientific foundation.

PREPARATION OF RADIUM

It may be of interest to briefly consider the methods of isolating the mineral from the various ores in which it has been found. The chief source is pitchblende or uranium oxid, found in various parts of the world. The principal workings are at Joachimsthal in Bohemia, but it is also found in Hungary, Saxony, Turkey, Cornwall, Sweden, and Colorado.

Three steps are used in the process of extraction of the element:

(1) *Mechanical,* in which, by crushing and pulverizing the ore, it is reduced to a very fine powder.

(2) *Chemical,* in which, by treatment with hydrochloric acid and carbonate of soda, a solution is finally obtained containing only radium and barium.

(3) *Fractionization:* By repeated crystallizations a more and more concentrated solution of radium salts is obtained until, finally, from one ton of ore, two to five centigrams of pure radium bromid are produced.

But pitchblende is not the only source of radium. Small quantities of it, much smaller than the amount in pitchblende, have been found in most minerals which contain thorium and uranium, and the rarer earthy metals also contain small traces of radium. It is found to occur, also, in certain mineral waters, and in the mud from hot springs, and, therapeutically, as will be seen later, this factor is of considerable importance.

CHEMICAL AND PHYSICAL PROPERTIES

When we speak of radium we mean one of its salts, usually bromid, chlorid, or sulphate. The element itself has only recently been isolated by Mme. Curie, and its properties have not, as yet, been sufficiently de-

termined. Radium has an atomic weight of 226, and is thus the third known heaviest element, coming after uranium and thorium. Its most distinguishing property is, of course, the possession in a higher degree than any other known substance of those properties called radioactive. These properties are four in number, viz.:

1. The liberation of heat.
2. The liberation of light.
3. Its power of ionization, that is, it renders air a good conductor of electricity by separating it into ions.
4. Its production of certain rays which can pass through opaque bodies, make impressions on photographic plates, and produce various biological effects.

Thus it can be seen that radium liberates an energy which shows itself in diverse ways. It is this energy which is made use of therapeutically, and it will therefore bear further study.

The energy given off by radium is complex and has been found to consist of: (1) A radiation composed of three distinct kinds of rays, which have been called the Alpha (α), Beta (β), and Gamma (γ) rays, and (2) the liberation of a gas, called the emanation.

Radiation.—The *Alpha* rays are made of atoms, that is, material particles of matter, about twice the size of an atom of hydrogen. They are positively charged and are projected with a velocity of about twenty thousand miles per second. About 90 per cent. of the total radiation is made up of Alpha rays. They have very little penetrating power and are easily stopped by a thin piece of paper or rubber. Owing to this slight penetrating power, the Alpha rays are not available for use in most of the forms of apparatus employed in treatment. Recently, however, by use of solutions of radium salts injected into tissues, the Alpha rays are being used, and, forming, as they do, such a large percentage of the total available radiation, this method of treatment is of great importance and will be discussed more fully later.

The *Beta* rays are made up of particles negatively charged, and projected with a velocity almost as great as that of light. In size they are about 1-1000 of that of the hydrogen atom, and in all respects except velocity are identical with the cathode ray particles liberated in a vacuum tube. Beta rays form about 9 per cent. of the total radiation, but are not all homogeneous, varying in their power of penetration. Some are very little more penetrating than the Alpha rays, and are known as "soft" Beta rays; others, called hard Beta, are extremely small and have great speed and penetrative power. Between these extremes are what are called the medium Beta rays, which range in ascending strength from the soft to the hard Beta rays.

The *Gamma* rays form only about 1 per cent. of the total available radiation. They have great penetrating power, traversing as much as

ten centimeters of lead quite readily. They have a velocity equal to that of light and are a pulsation of the ether, in this respect being similar to X-rays. But they differ from the latter in their greater power of penetration. On encountering matter the Gamma rays produce secondary rays, similar to Beta rays. These were first described by M. Sagnac and are usually called after him. Therapeutically this is a point to be remembered, as many secondary effects, such as telangiectases, may be produced if these secondary rays are not guarded against.

Owing to the differences in penetrative power possessed by different rays we are enabled, by interposing suitable screens, to use what rays we wish in a given case. Thus a very thin screen of paper or rubber will serve to cut off the Alpha rays, allowing only the Beta and Gamma to pass. With screens of different density, made of aluminium or lead, the different Beta rays can be intercepted, the thickness of the filter determining whether the soft or hard Beta rays will be cut off, until finally by interposing a lead screen of at least 5 or 6 millimeters in thickness only the Gamma rays pass.

Emanation.—In addition to the radiation, radium gives off energy in the form of a radioactive gas called the emanation. This is only given off freely when the radium salts are dissolved in water. It is a true gas which chemically belongs to the Argon group of inert gases and has an atomic weight of 222. The emanation is intensely radioactive and gives off at first Alpha rays, then Beta rays, and later Gamma rays. However, its radioactivity does not last long. It is decreased by one-half in four days, and it almost completely disappears at the end of the month.

The emanation has the power of conferring radioactivity on those bodies with which it comes in contact. Up till recently the emanation was not used in therapeutics, but recent researches have established its efficacy and a means by which it can be properly applied.

METHODS OF APPLYING RADIUM

The question how to apply radium salts to the best advantage is a very large one. Several factors necessarily come into consideration. It is desirable to use an apparatus which will give an even distribution of radiation, and one in which every particle of radium can be used to the best advantage. On occount of its great cost one naturally desires a stable form of applicator, one that will not be impaired by contact with the body tissues. The earliest containers were glass tubes or capsules. These had the manifest disadvantage of being easily broken with loss of some of their contents. Moreover, in a tube the particles of radium naturally collect together at one end, so that a great deal of the radiating surface is lost. The chief advantage which these tubes possessed was

the facility with which they could be inserted into tumor masses, or passed into the various body cavities through either natural or artificial openings. At present we still use these tubes, only now a silver or, preferably, a platinum tube is used as a container. These can be obtained holding various quantities of radium bromid, from a milligram to 2 or 3 centigrams. Their chief sphere of usefulness lies, as is said above, in the facility with which they can be inserted into small openings. In using the tubes this way I employ a method suggested to me by Dr. Robert Abbe, of New York. The radium tube is threaded on a silk or silver thread and passed into a celluloid tube some four inches in length and about a quarter of an inch in diameter. The celluloid tube in no way diminishes the radiation, which, after passing through the platinum capsule, consists essentially of hard Beta and Gamma rays, while it pro-

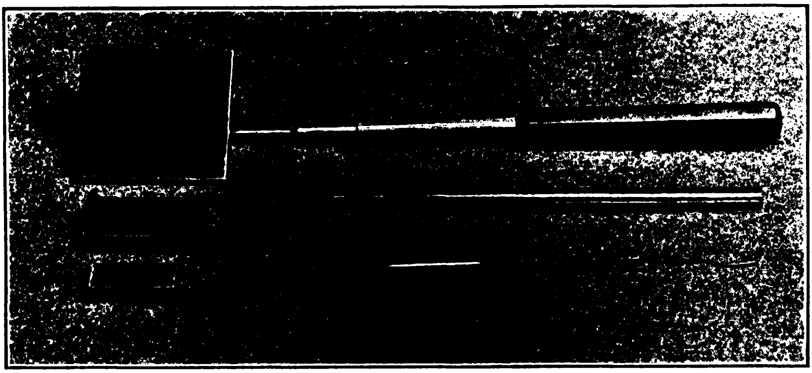

FIG. 1.—SOME RADIUM APPARATUS. (Author's Collection.)—Nos. 1, 2, 3, and 4, radium plaques ranging from 50,000 to 500,000 activity and of different sizes from one to four centimeters square. No. 5, celluloid tube devised by Robert Abbé of New York, to contain a tube of radium for insertion into tissues. No. 6, small platinum tube containing 1 centigram of pure radium bromid (2,000,000 activity).

tects the capsule from contact with, and more or less disintegration by, the body fluids. The celluloid tube, with its contained radium tube, can then be introduced into various situations, such as new growths, into the bladder, rectum, etc., etc.

For the application of radium salts to more extensive surfaces Dr. Wickham devised a method of incorporating the salt into a varnish, which was then fixed to a metal or linen base ("toile" applicators). The varnish used is a special one which procures great solidity and permeability. This is poured into the base, which is usually made of copper, and the required amount of radium salt is spread over the surface so as to obtain as even a distribution as possible. The varnish is dried and resined, when it presents a hard, smooth, shiny surface. At first the radium grains appear as yellowish specks, but they soon become brown, and finally black. "The radioactive value of the varnish naturally de-

pends on the quantity, quality, and proportion to the surface of the contained radium." These "plaques," as they are called, can be obtained in a variety of strengths, shapes, and sizes, depending on the particular part of the body to be treated. Not nearly so much of the radiation is lost as in the case of tubes, and a large proportion of the softer Beta rays, and some few of the Alpha rays, can escape and exert their peculiar actions. The "toile" applicator consists of a cloth covered with radium varnish. A much larger proportion of Alpha rays escape. The apparatus is flexible and can be molded to any particular part of the body, around a limb, for instance. It is usually employed where short applications of a strong radioactivity are desired over a fairly large area, as occurs in certain skin diseases.

Dosage of the Radiation.—The radiation from the apparatus may be varied both quantitatively and qualitatively, depending on the effect desired. Thus, if a superficial action is necessary, as is found in certain skin affections, short applications of a naked plaque are used. By the term "naked" is meant that no screens are employed to cut off certain of the rays. It was seen that the various rays had different penetrating power. The Alpha rays are practically all blocked by the varnish with which the salt is incorporated. To stop the Beta rays screens of aluminium 1-10 millimeter, or more, in thickness are used, depending on what quantity of the softer Beta rays it is desired to obstruct. The medium Beta rays are only stopped by screens of lead varying in thickness up to one-half millimeter. A screen of this density allows only the hard Beta and Gamma rays to get through. As these rays form a small percentage of the total radiation it is necessary to leave such an apparatus on for some hours, all night, for instance, in order to get the effect of the Gamma rays on the deeply lying structures. When using metallic screens it must be remembered that in passing through them secondary rays, rays of Sagnac, are produced, which have a superficial irritating action. These are cut off by placing a few sheets of thin paper, preferably black, over the screens next to the surface to which the plaque is to be applied. Over the whole a thin sheet of rubber is then applied. The rubber should be used in every case, even when the apparatus is used "naked," as it serves the double purpose of protecting the varnished radium surface from destruction by skin secretions, exudations, etc., and, a fresh piece being used for each patient, the ordinary esthetic rules of cleanliness are complied with. For this purpose the thin rubber sheeting known as Dental Rubber Dam is excellent. The radium plaques are fastened over the parts where their action is desired by means of strips of adhesive plaster.

"Cross-Fire."—What Wickham calls the "cross-fire" method of application is one found to be exceedingly useful in practice. Here, by placing apparatus at different points, the rays can be made to cross each other in various directions, and the tissues are thus inundated with the

energy. When placed on opposite sides of a tumor, for instance, the tissues midway receive by this method twice as many rays as if the apparatus were only on one side, and there is a more even distribution of the rays throughout the mass.

The strength of the apparatus one is using is, of course, a necessary factor to be considered in directing the treatment. It is usually measured by the radioactivity produced by it. Uranium being taken as the standard and given a radioactivity of 1, the radioactivity of pure radium is 2,000,000. The radioactivity is measured by the relative speeds with which a charged electroscope is discharged when a radioactive body is brought near to it. Pure radium is employed therapeutically only in the forms of the tubes or capsules mentioned previously. On the varnished plaques radium is mixed with an inert body, usually bromid of barium, in varying proportions. Thus a mixture of one part of radium and three parts of barium bromid would have an activity of 500,000, a strength quite commonly used. Other apparatus is prepared with a strength of 100,000, 50,000, and so forth. With the apparatus as purchased one receives a certificate of the amount of radium salt and its strength. This should be verified by means of the electroscope, and tested again from time to time during the first few months until the apparatus is matured.

It has been suggested by Turner that the dose of radium should be "stated in terms of the product of the strength of the preparation and the length of the exposure—what would be termed in an electrical measurement the 'ampere hours.' Thus a ten-milligram specimen applied for one hour would be called ten milligram hours; applied for thirty minutes, five milligram hours. If five milligrams were applied for twelve minutes it would be one milligram hour, and so on. Thus a dose of ten milligram hours could be given by one milligram applied for ten hours, or twenty milligrams for thirty minutes, etc."

Such a method as this does not, however, take into account the area of the surface or plaque on which the radium salt is distributed. This factor is one of great importance, as considerable difference in the method used occurs, depending on whether one is using a small tube containing ten milligrams of pure radium, or whether the ten milligrams is spread out on a surface of sixteen square centimeters and has its activity lessened by being mixed in various proportions with inert barium salts.

So far there is no fixed standard of measurement, and, in using the various apparatus as they are prepared at present, it is better to simply say one is using a tube of a certain amount of radium, or a plaque of a certain size covered with radium of a known radioactivity.

Dosage of the Emanation.—When radium is employed in this way, the element itself is spent, being usually injected into the tissues. The Alpha rays, which constitute 90 per cent. of the total radiation, are here made use of and set up an induced radioactivity in the tissues which

lasts for a considerable time. Very small quantities of the salts are used, so that the expense is not so great as one might be inclined to think. The scientific use of radium injections is at present being investigated by Dr. Wickham, to whom the writer is indebted for a description of his methods.

As was mentioned above, the most usual way of employing the emanation is by the injections of soluble salts (bromids) or of insoluble salts (sulphates) of radium into the tissues, in water, or other vehicles. The dose is 1 to 10 micrograms, a microgram being the one-millionth part of a gram, in one cubic centimeter of water. Five to ten injections are given during ten to twenty days.

The emanation may also be given in the form of ingestions, such as in quinin, or various colloidal substances containing radium, as radioactive mineral waters, which lose their radioactivity during shipment, but can have it restored by the addition of a given dose of radium.

Radiferous mud, which is what remains of uranium ore after the extraction of pure uranium, is also used, as well as the natural mineral muds. These are very weakly radioactive, and what activity there is is produced more by actinium than by radium. It has been found that these muds really act through the liberation of the emanation into the atmosphere and this is then inspired by the patient. Baths of radioactive waters act in the same way.

The Use of Radium Ions.—One other way of using radium must be mentioned, although it has not developed fully enough, as yet, to enable one to judge of its ultimate results. This is the introduction into the tissues of the radium ion in the same way that other salts, such as those of zinc and copper, have been used. A continuous electric current of 10 milliamperes is employed. A compress of linen saturated with a solution of bromid containing 10 micrograms of the salt per c. c. is placed over the diseased area and covered with the positive pole. The negative pole is placed on the other side of the tissues. The current is allowed to pass for half an hour and the radium is introduced into the flesh, where, without the least injury to the skin, it has been found acting at a depth of 5 to 9 centimeters.

The radium accumulates in considerable quantities, and may remain *in situ* for fifteen days without causing any damage to the healthy cellular elements. Clinically, as has been mentioned, this method is in its infancy. At the time of writing a case of sarcoma was reported as being greatly reduced. It is a method which would appear to have great possibilities before it, provided a too strong solution of radium is not required, when the question of expense would naturally arise.

USE OF RADIUM IN THERAPEUTICS

Histological Changes Induced by Radium

Having discussed the nature of radium and the energy to which it gives rise, together with the methods we have of making use of this energy, we now pass on to a consideration of the use of radium in therapeutics, but, before doing so, it may be profitable to investigate the way in which the tissues are affected histologically by radium, so that the nature of the radium reaction may be better understood.

This reaction varies considerably, depending on the nature of the rays used and the length of exposure given, so that, on the one hand, we can produce destruction, with subsequent inflammatory reaction, and, on the other, so gauge the apparatus and time of exposure that we may obtain what Wickham has called "selective action," the word "selective" meaning simply that special pathological cells have an inferior resistance to the radium rays. This latter action is what, in the majority of cases, it is desirable to obtain, but, owing to the fact that radium reaction was first discovered by Becquerel from a severe burn which resulted on his abdomen after carrying a tube of radium in his waistcoat pocket, the common view is, that all radium can do is to produce a burn, like many other caustic agents. This destructive action is, however, important also, as many conditions can be treated by this means which do not respond to selective action. As a rule, probably a combination of the two types of reaction is most suitable, as in this way the time element, often of great importance, can be greatly shortened.

Dominici and Barcat have made extensive investigations on the histology of the reaction, and, as this work is regarded as authoritative and has been freely quoted in the few text-books on radium extant, we cannot do better than make use of the article in question, which was published in the *Archives des Maladies du Cœur, des Vaissaux, el du Sang.* After exposure to a varnish apparatus of 500,000 activity for ten applications of five minutes each, the skin of a guinea pig is found to become red in ten days. In twenty a slight ulceration develops and a crust forms over it. This falls off after about five weeks, leaving white skin without hair or pigment. Histologically there is an hypertrophy of the epidermal cells with edema; the epidermis is subsequently detached and the hair follicles, sebaceous and sweat glands undergo atrophy and are not reformed, though the epidermis is. In the corium, also, changes are to be observed, for the connective tissue bundles and elastic fibers have disappeared almost entirely and their places are taken by an embryonic form of connective tissue resulting from a multiplication of the fixed cells. These cells line the walls of cavities filled with red and white

corpuscles, and, in fact, are endothelial cells lining the small vessels which have been transformed into embryonic capillaries. These latter extend by budding, and eventually form a vascular connective tissue, which has been produced without ordinary inflammatory reaction. The cellular elements predominate over the vascular, and in further development the capillaries are practically occluded, so that there results "a sort of flat, fibrous tissue, the fixed cells of which preserve in many particulars a conformation similar to that of the myxomatous tissue. Thus the final cicatrix is gradually produced, a cicatrix having neither the structure of the corium of normal skin nor that of post-inflammatory sclerotic tissue. Its texture differs from that of the corium of normal skin, the newly formed connective-tissue bundles and the cells which separate them being regularly superimposed and forming lines parallel to the surface of the body. This arrangement differs from that of the adult corium of the regular type, which is a collection of connective-tissue bundles, crossing one another in every direction, and forming a boundary to fissures, in which are placed sparse fixed cells having an uncertain direction. The structure of the cicatrix differs from that of the sclerotic post-inflammatory tissue by its regularity, its uniformity, the absence of fibroid perivascular rings and of vascular obliteration. It is composed of connective-tissue bundles separated by elongated fibroblasts. The fibroblasts and connective-tissue bundles are parallel, both to each other and to the surface of the skin. The fixed cells become rarefied six or seven months after the beginning of the experiment; their substance and nucleus grow smooth, while their chromoplasm disappears, becoming changed into hyaloplasm; the anastomoses which unite them cease to be visible and the connective-tissue bundles separating the layers of fibroblasts thicken, while the elastic fibers reappear in increasing proportions, those portions of the derma which have been subjected to the influence of radium being differentiated from those not affected by it by the alteration and regular direction of the connective-tissue bundles and fibroblasts. Their texture is analogous to that of a flat fibroma with connective-tissue bundles and stratified cells arranged in a regular manner."

"*Action of Radium on the Histological Process of Inflammation and of Connective-Tissue and Epithelial Tumors*

"Radium rays are capable of modifying diseased as well as healthy skin. It is for this reason that experimental cutaneous tuberculosis of the guinea pig, certain atypical sarcomata of the human skin, and also epitheliomata, can be healed by means of complete transformation of sarcomatous tissue into tissue of a fibrous nature.

"**Experimental Cutaneous Tuberculosis.**—The action of radium on cutaneous tuberculosis is characterized by three phenomena, viz.:

"1. Diminution of the simple inflammatory perituberculous reaction (disappearance of the accumulation of the polynuclears of macrophagocytosis, transformation of lymphatic cells into plasma cells, and development of nodules possessing a lymphoid structure).

"2. Organization of the vascular connective-tissue stroma, which was the seat of this simple inflammatory process.

"3. Extension of this process to the tuberculous follicles themselves, the epithelioid cells of which lose their globular conformation, elongating and anastomosing in a network of fixed cells of embryonic type.

"As a result of this the epithelioid tissue of the tubercles is changed —at least in part—into embryonic myxomatous tissue. The cure is completed by the transformation of myxomatous into sclerotic tissue having a texture identical with that of a pure fibroma.

"**Sarcomata.**—The retrogression of atypical sarcomata takes place—at least in some instances—according to the law which we have just formulated. The size of the body and of the nucleus of its enormous cells gradually decreases. As they shrink the neoplastic elements elongate, the contours of their nuclei become regular, and they finally assume the form of large embryonic connective-tissue cells, anastomosing in a cell mass similar to that of the myxomata. The resemblance is the more striking as they are surrounded by myxoid tissue, in which connective-tissue fibrils are gradually developed. The tissue of the sarcoma is thus transformed into myxomatous tissue, which ultimately changes into tissue resembling that of a fibroma.

"**Epitheliomata.**—Under the influence of the radium rays, the cells of cancroids of the skin or of the mucocutaneous regions (the lips) gradually diminish in size. This atrophy corresponds, not to the metamorphosis of these definitely formed elements, but to their destruction. The epitheliomatous cells disappear, either by means of a progressive absorption of their protoplasm and nuclei, or by a sort of granular dissociation of the two parts forming the cell. During this time the inflammatory processes which accompany the development of every epithelial tumor are arrested, while the vascular connective-tissue is organized according to the method which has just been described."

The action of radium on the liver was studied histologically by Mills. An apparatus of 500,000 activity was used, so screened as to cut off the Alpha and Beta rays. Exposures of thirty minutes were given. The results were that within one hour of the exposure an appearance occurred in the hepatic cells, resembling "cloudy swelling." Subsequently an inflammatory reaction, which lasted only a few days, took place, and this was followed in about two weeks by a later inflammatory reaction, confined to the connective-tissue elements and consisting of an infiltration with lymphocytes, a few polymorphonuclear leukocytes, and fixed connective-tissue cells.

In regard to the cutaneous reaction, it is occasionally found that when destructive and not selective action alone is used there may result in the scar telangiectases or pigmentation. In a large majority of cases this causes no particular anxiety, but when treatment has been undertaken for some cosmetic reason, such as the removal of a small nevus or keloid, it is important to avoid anything which would detract from the result. The secondary rays of Sagnac, caused by the passage of Gamma rays through metal screens, often seem to be the cause. This can be prevented by using screens of paper over the metal.

Therapeutics

As Sir Malcolm Morris has aptly expressed it, the history of radium therapy might well be divided into two periods—"before Wickham" and "after Wickham." It is true that to Dr. Wickham the medical world owes a scientific, impartial investigation into the action and method of applying radium. As director of the Radium Institute in Paris he has had great opportunity to prove or disprove the reports of other observers, so that what he says can be taken as established. From the results of his work, which has been corroborated by others, it can easily be seen that in radium the profession possesses an agent which, if properly controlled, can be of inestimable benefit in many conditions, both malignant and non-malignant. It is no panacea, as some claimed at first, for all malignant growths, and, as yet, in fact, the limitations of its powers are not fully known. Much, however, has been established, and we believe that we may confidently expect the sphere of its usefulness to increase rather than the reverse.

Like all new agents, radium has been used experimentally in a great number of conditions, and with excellent results in a large number of cases. In the treatment of new growths and in dermatological practice its widest field of usefulness has as yet been manifested, although recent literature would point to the beneficial use of the emanation in many conditions of metabolism, such as gout and chronic rheumatism.

Gout, Rheumatism, and Allied Affections

The use of radium in internal medicine is still very much in the experimental stage, but very definite results have been obtained in the treatment of those painful conditions whose etiology is as yet so indefinite, but which are commonly spoken of as due to chronic gout or rheumatism and are associated with the so-called "uric acid diathesis." Experimentally it has been shown that the dissolution products of radium emanations are able to render monosodium urate more soluble by decomposing it into

carbonic acid and ammonia, and where artificial tophi have been produced in animals, which have subsequently been confined in a chamber exposed to radium emanations, histological studies have shown that the emanations almost entirely prevent the reactive leukocytic infiltrations and that the monosodium urate is rendered much more soluble.

The subject of the use of radioactive substances in this connection is a very large one, for it has been found that many of the waters from certain springs famed abroad for their great benefit in many diseases of metabolism are radioactive, and the inference is drawn that the benefits derived from the drinking of and bathing in these waters have been due to the presence of radioactive matter. The radioactivity is present in the form of the emanation, which, as we have seen, is a gas, and which soon passes off after the water is removed from its source. This apparently accounts for the less satisfactory results which follow the use of the same waters after being bottled and transported to various points.

When radioactive matter has been added to indifferent waters they become therapeutically active, and this has led to the employment of various devices for the use of the emanation from radium itself. At Joachimsthal, where the great radium mine is situated, Gottlieb noticed marked results among the miners working among the pitchblende. Many other clinicians have recorded similar observations, which have been thus summarized by William Armstrong, of Buxton:

1. Greatly increased diuresis and excretion of uric acid.
2. Largely increased carbonic acid exhalation.
3. Lowered blood pressure.
4. Decreased blood viscosity.
5. Increased activity of peptonizing and diastatic ferments.
6. Enhanced autolysis.
7. Prevention of the transformation of the easily soluble lactimurate (mononatriumurate) into the less soluble lactimurate.
8. Marked solvent action on gouty deposits.
9. Excretion of uric acid took place as promptly in gouty patients as in healthy individuals, overcoming the special difficulties of the gouty, namely:
   (a) Retardation of purin body metabolism.
   (b) The slowing of the formation and of the breaking down of the uric acid.
   (c) The alteration in the mutual relation of the two processes.
10. The dissociation of uric acid and its salts into carbon dioxid and ammonia.
11. Inhibition of inflammation and relief of pains in rheumatism.
12. Increase in sexual vitality.
13. Considerable influence over sympathetic nerve affections, such as neurasthenia and allied conditions.

14. Marked results in diabetes, albuminuria, and glycosuria.

In gout, according to His, the most striking results are obtained, due to the chemical reaction induced by the radium. It is most important, therefore, from the standpoint of prognosis that one should be quite certain that one is dealing with a case of gout and not of chronic rheumatism, where the results are not so good. This, of course, is not always an easy matter. Nor must one expect miracles to be wrought and think that a joint in which anatomical changes of a severe nature have occurred can be restored to normal. While using this treatment one must not neglect the important hygienic and dietetic procedures of such great value in these conditions.

In the treatment of these affections the greatest benefit has been derived from the use of the emanation, which is a gas, and can be taken into the body with the inspired air, or absorbed from the digestive tract. In using baths the emanation passes out into the air and is breathed. It cannot pass through the skin of the body. This gas is excreted through the kidneys and through the lungs. It can easily be seen that in the form of baths the patient only receives emanation while he is in the bath, or the room where the radioactive water is exposed. On the other hand, when taken into the alimentary canal there is a slow absorption of the gas, and one dose provides emanation sufficient for three or four hours. It has been found that when the patient has been given from three to five doses during the day, the emanation can be detected in the expired air at any time.

For the use of radium emanation at home various devices (known as "emanatores") have been constructed. The principle of the apparatus is very simple. There is a large flask containing radium in solution. Air which is passed over this becomes laden with the gas, and is then inhaled by the patient.

When used in any of these forms the action is a general one. For the local use of the emanations injections of radium salts into the neighborhood of the joints affected have been utilized. Thus a local focus is created from which the gas is continually being given off for some time.

Dermatological Practice

There is a very large field of usefulness for radioactive substances in the treatment of many diseases of the skin. Radiation as produced by X-rays has, of course, been used with very good effect for years, but the introduction of the newer bodies, and the ease with which they can be handled, has given us therapeutic agents which are of inestimable value.

Radium has been chiefly used, but recently salts of thorium, of much less activity, have been reported to give results, and various synthetic radioactive products have also been described. As it is radium with

which we are concerned here, and as the literature is more extensive in regard to it, we shall only describe methods and results obtained from its use.

Lupus Vulgaris.—In these lesions radium can be used with good effect, but it exerts no selective action, the result depending on the facility with which destructive action can be caused when unscreened plaques are employed. Heavy doses should be employed to produce a strong reaction. Not only the actual lesion but the tissues about it should be subjected to the treatment to avoid recurrences. As regards results, radium is no more effective than the Finsen light, but the treatment is not nearly so prolonged, and, in cases where the lesion is inaccessible to other methods, as in the nasal cavity, for instance, radium has a distinct advantage. Moreover, the scar left by radium is much more esthetic than that produced by any other method.

Lupus Erythematosus.—This most chronic condition frequently has given excellent results with radium. Here again fairly strong doses must be applied, and to the surrounding tissues also. Wickham and Degrais report a case in which injections of radium bromid were used with very good effect.

Eczema.—Chronic eczemas can be relieved after all other methods have failed by short applications of plaques or toiles of low activity. It is in these conditions that the toile has its greatest field of usefulness, for a whole limb or portion of it may be wrapped up for a few minutes. Other treatments, both local and constitutional, must not be lost sight of at the same time. One of the first results is usually the relief from the intolerable itching which accompanies these conditions. Bayet reports 41 out of 42 cases successfully treated. In acute eczemas slight exposures are also of great service when there is a tendency to recurrence. Five-minute applications of an unscreened plaque are sufficient, and these can be repeated as necessary.

In the case illustrated an apparatus of large surface and with an activity of 600,000 was used, with a very feeble filtration. The apparatus was left in contact with the surface from one to three minutes. The next day and the day after the same apparatus was used, then followed an interval of non-treatment for eight days. In this way twenty-seven minutes were given, and in the course of two weeks more the skin returned to a normal condition.

Psoriasis.—Resistant patches of psoriasis are successfully treated by short applications of a naked plaque. When used on the face a light aluminium screen may be used to avoid pigmentation. In eight to ten days the scales fall off, leaving a slight stain which soon disappears.

Acne Rosacea.—With short exposures obstinate cases of this disease may very frequently be cured after other methods have failed. Bearing in mind the cosmetic effect desired, the plaque should be covered with

FIG. 2

ECZEMA OF THE ARMS. BEFORE TREATMENT. APPEARANCE TWO WEEKS LATER.
(Collection of Wickham and Degrais.)

a light aluminium screen and five to ten sheets of black tissue paper, so as to avoid inflammatory action, and the cases should be treated cautiously, using short exposures and giving sufficient time between the series of treatments.

Acne Vulgaris and Acne Keloid.—In the same way chronic cases of acne vulgaris may be treated, particularly when much scarring is present. In the condition known as acne keloid, where there is development of keloidal tissue in acne scars, and which is usually situated on the nape of the neck, radium is most beneficial, as we shall see it is in the treatment of keloid elsewhere. Screened plaques should be used.

Parasitic Diseases of the Skin.—In such conditions as sycosis of the beard or ringworm of the scalp, radium will be found of great benefit, just as the X-ray has been found to be so beneficial. These refractory lesions will clear up in two or three weeks after receiving radium exposures. Only short applications of unscreened plaques are necessary.

Analgesic Action of Radium.—In localized pruritus rapid benefit is obtained by the use of radium, the itching ceasing in one or two days.

In pruritus ani probably the greatest relief is given, but pruritus vulvæ or pruritus of the scrotum are also greatly benefited.

The analgesic action of radium is further manifested in the good effect it produces on the severe pains which so frequently follow herpes zoster. Two actions are to be obtained in these cases. Heavily screened plaques are left *in situ* over the tender points all night or for two or three successive nights in order to influence the deep branches of the nerve, while shorter applications of two or three hours, lightly screened, are used to affect the superficial nerve terminals. Used in this way great relief is experienced in the course of a few days.

Hypertrichosis.—Radium rays properly used will destroy the hair follicles and remove the excessive growth of hair sometimes so disfiguring to a woman. By using a light lead screen covered with paper, one can frequently destroy the hairs without producing any marked irritation to the skin. Exposure to the harder rays, as one would get in this case, may be as long as two or three hours, and should not be repeated before twelve or fourteen days—to see what reaction takes place. By shorter exposures to the naked plaques the hairs are also removed, but here more irritation is produced and pigmentation may sometimes take place afterward. For its ease of application, both to the patient and the physician, in these conditions, radium excels other methods of treatment.

Keloids and Cicatrices.—A distinction must be made between these two conditions, for the true keloids give much more satisfactory results than does simple cicatricial tissue. Wickham claims that the keloid reacts in a selective way to radium, whereas the normal cell is not so acted upon. In the keloid we have the choice of two methods of treatment: the destructive, using naked plaques and getting a severe superficial reaction, or, by the use of screened plaques and longer exposures, producing a gradual absorption and disappearance of the deformity without visible signs of reaction. In large keloids the "cross-fire" method is often of considerable service, and it must be remembered that the periphery of the growth should be well influenced, for the prolongations often extend further than they are visible. Prominent cicatricial tissues not of keloid nature, such as are so often seen following a cervical adenitis, can only be leveled by causing considerable destructive action. Here the results are not apt to be so satisfactory as in the case of keloids. In the treatment of the latter radium can almost be regarded as a specific, when it is considered how little amenable they are to other forms of treatment.

Angiomata and Nævi.—These conditions offer themselves very readily for radium treatment, and the result is, in a large majority of cases, most satisfactory from an esthetic standpoint. The duration and strength of the applications vary considerably with the local lesion. In a superficial port-wine stain our efforts should be directed toward producing a gradual fading with practically no visible reaction. By doing this subsequent

telangiectases and white depressed scars are avoided. The best results have been obtained with plaques or toiles of an activity from 50,000 to 100,000 lightly screened with 1-10 mm. of aluminium, this again being covered with eight or ten sheets of black paper, to cut off the secondary rays of Sagnac. Each individual case must be experimented with at first to see just how long an application can be given. Probably three hours divided into three sittings of one hour each will be found sufficient to produce, in the course of four or five weeks, a very slight superficial desquamation. Further applications can subsequently be made, bearing in mind the fact that tissues once radiated are more sensitive to subsequent applications, so that so long an application will not be necessary for further treatments. The effect in these cases often extends over some months, so that gradual fading may be looked for even after reaction has

FIG. 3.

ANGIOMA BEFORE TREATMENT. APPEARANCE THREE MONTHS LATER.

(Author's Collection.)

ceased. The whole treatment may last two or three years, as the watchword must be not to hurry for fear of subsequent ill effects.

When the condition is more vascular and forms a moderately raised angiomatous tumor, different methods can be used. In this group pulsatile angiomas are not included, but those in which there is a fairly large amount of fibrous tissue, so that the tumor is firm to the touch. Here stronger destructive action may be best employed, using unfiltered rays and making exposures of three or four hours. By using filters and increasing the duration of application the same result may be obtained without so much reaction. Here also the "cross-fire" method may be employed to advantage if there is a large enough mass, apparatus being placed on opposite sides of the tumor, inundating it with rays. From a cosmetic standpoint the results in these cases are often not ideal, as some evidence of the blemish usually remains, which, however, in comparison with the former disfigurement can be practically disregarded.

Again, the individual factor plays a large part, and an apparently similar condition in one patient will give a much better result than it will in another. Here again, as so often occurs in the case of rodent ulcers, the results with radium are found to be not so good if previous electrical treatment has been used, resulting in the formation of scar tissue.

A third group of these lesions comprises the softer vascular and pulsatile angiomata occurring on the skin or mucous membrane. In all these destructive action must be avoided, as there is considerable danger of producing hemorrhage. With these conditions others belonging to the two previous groups are often found, so that a combined lesion is present of which the individual factors must each receive its appropriate treatment. It is in these conditions that Wickham and Degrais have had the greatest success with the "cross-fire" method. Fairly strong plaques lightly screened with 1-10 mm. of aluminium, and applied for five or six hours in divided doses of one hour each, every other day, would constitute sufficient dosage for the first series. Depending on the result from this one can gage whether more or less should subsequently be given.

The case illustrated is one which combines all features of the angiomata. The skin was of a deep purple-red, studded as can be seen with tubercles. There was considerable involvement of the lip, extending through to the mucous membrane. On pressure the blood could be driven out to a certain extent but not entirely, None of the tumors pulsated. It was one of my early cases, and the patient had come a considerable distance, and had only a limited time at his disposal. We were both therefore anxious for a quick result, and more radiation was used than one would have been inclined to employ could the dosage have been repeated every few weeks. As a result fairly severe reaction took place, which was rather painful for a short time, but that it produced results can be seen from the other photograph taken about three months later. The nodular appearance is nearly all gone, the distorted lip has greatly improved, and the color has faded to a considerable extent. Further treatment should of course be given, but the improvement which has already taken place is such that the patient is more than satisfied with the result.

Radium in these conditions has the advantage over other methods of treatment, such as surgery, electrolysis, and X-rays, that it can be so easily applied, and that it is practically without pain, two factors of particular importance in the case of children. Moreover, the subsequent appearance is better than can be obtained by other means, the scars being hardly distinguishable from the surrounding skin, and not white and depressed like those after carbon dioxid snow and other methods.

Goiter

As the radium rays have such an influence in checking glandular activity, together with a production of connective tissue, one might expect that in certain conditions of the thyroid gland radium would be of

service. This is a field to which very few radium therapeutists seem as yet to have devoted themselves. Robert Abbe, of New York, some few years ago reported a case of exophthalmic goiter in which, by burying a radium tube through an incision in the gland, there was a marked shrinkage in the size of the thyroid and a great improvement in the general symptoms. Wickham, of Paris, has also reported a case of Graves' disease apparently cured by the exposure of the gland to strong radiations from the plaques, the cross-fire method being used. The writer has had a number of cases in his own practice which have shown the good effects obtained in certain conditions of this gland. Cases of hyperthyroidism have been greatly benefited, the symptoms being checked and the gland diminishing, as exhibited by the circumference of the neck, from one to two and a half inches. Other cases of ordinary parenchymatous goiter have shown similar retrogression. To effect this, the "surpénétrant" radiation must be used and the plaques left in position from ten to twelve hours, repeated daily or every other day, so that one hundred or more hours may be given. Over the lead screens paper should be placed to avoid discoloration of the neck by the induced rays of Sagnac.

Gynecology

Apart from the treatment of malignant disease considered elsewhere, it would appear that radium has an action which is of great benefit in many other conditions encountered in gynecological practice. This is due to several factors. In the first place, the apparatus for applying radium and the methods of using it are such that uterine conditions can be treated with great facility. For instance, a tube of radium can be easily introduced through the os into the cervical canal, or even into the body of the uterus; or by the use of properly screened plaques the action of "surpénétrant" rays may be obtained upon the pelvic organs, without any effect on the skin of the abdomen. In the second place, the analgesic and hemostatic qualities of radium find a particular field of usefulness in gynecological conditions. The matter has been investigated chiefly by Drs. Oudin and Verchère, and from the results so far obtained they feel justified in claiming for radium a distinctly alterative and beneficial effect in chronic inflammatory conditions, and a very useful hemostatic action in the treatment of uterine fibroids. Using ultra-penetrating rays a tube may be left *in situ* for three to five hours, and this dosage may be repeated two or three times a week.

Ophthalmology

For certain external conditions affecting the eyes and eyelids radium has been used with remarkable success. To Drs. Mackenzie Davidson

and Arnold Lawson we are indebted for the most of our knowledge of its results in ophthalmological practice. In applying radium the eye is first anesthetized, and the apparatus is so screened that only the harder Beta and Gamma rays are allowed to act. Owing to the difficulty of fixing the apparatus (in the form of tubes) in place, it is better for the operator to hold it in position, and his fingers should be protected by a wrapping of thick lead foil. Short applications are desirable for fear of causing inflammatory reaction, although this has not been observed even when the stipulated time has been exceeded. It is said that slight transient pain sometimes follows, but it is never severe. A large proportion of patients experience no pain at all. In one of rodent ulcer affecting the lid, Davidson found that a tube of 30 mg. of radium could be applied to the inner surface of the lid, and lie in contact with the sclerotic for half an hour without producing the slightest ill effect. In general the total dosage is regulated by the character of the lesion to be treated, so that "one exhibiting a tendency to spread or infiltrate surrounding tissues, or marked by any special virulence in its progress, would probably require a larger dose than a small, superficial, or non-infiltrating lesion."

Spring Catarrh.—In spring catarrh, a very chronic condition and very refractory to treatment, probably the most striking results have been achieved. The exact dosage cannot be stated, as we must be guided by the character of the lesion and the results of treatment. Five-minute applications of a capsule containing one centigram of radium bromid would be sufficient to begin with; this should hardly be repeated in less than one week. Davidson regards the action of radium in this condition as almost a specific. The scars produced are smooth and supple and do not tend to cause deformity from the contraction of the cicatrix. They are very bloodless, however, and after cure the tarsal surface of the lid is quite blanched.

When the immediate discomfort, if present, has stopped, the patient's subjective symptoms are, as a rule, relieved, the action of the radium producing here, as in many other conditions, an anesthesia of the parts.

Corneal Ulcers.—When stimulated by radium these heal much more rapidly than when not so treated. That this is a fact seems to be well established by the series of cases exhibited by Lawson and Davidson, where 16 out of 17 improved rapidly after treatment was commenced. In interstitial keratitis radium has been of benefit, there being much less corneal opacity resulting than when it is not used. It has also been of distinct benefit in cases of recurrent keratitis profunda and recurrent inflamed pterygium. Darier in France has been successful in the treatment of trachoma by the use of radium.

Although this is a field in which comparatively little has been done, still from the knowledge we have it would appear that radium is an agent of inestimable value to the ophthalmic surgeon.

The Treatment of Malignant Disease

Superficial Epitheliomata of the Skin.—Under this heading are included rodent ulcer and fungating cutaneous epitheliomata. The *rodent ulcer* is a lesion where the action of radium can be studied to the best advantage, as this condition reacts admirably to radium rays. It is here that one sees at its best what Wickham has called the "selective" action of radium. By using short applications of unscreened apparatus the ulcer will, in the course of ten days to two weeks, crust over, and after the crust has been removed the skin beneath is found to be healed over and a very smooth, non-depressed scar is left, which, in a short time, can hardly be distinguished from the normal skin. In very small ulcers this change can occur with practically no inflammatory reaction. In larger and deeper ulcers the same change can be brought about in the same way, but here the process, if treated without reaction, takes much longer, and when time is an important factor, as it often is to patients coming from a distance, it is better to use stronger doses, producing a destructive action.

It is a difficult matter for one to formulate set rules in regard to the length of exposure. It varies so much with the exact local condition, and the factor of the individual has to be considered as in any other branch of medicine, for one very seldom finds two persons who react in the same way. The plaque is the best form in which to employ the radium for this condition, using one of 100,000 activity, containing four milligrams of radium, and giving exposures of one hour each on four successive days. It is always well to use a plaque slightly larger than the area of the ulcer, as any outlying foci which have not as yet declared themselves may be destroyed. In many such cases one series will be sufficient, and after the scab has fallen off the skin will be found healed. During the time of the formation of the scab, and while it is present, no treatment is, in the majority of cases, necessary. Leave the scab alone and let it detach itself when ready. If, however, as sometimes happens there is some suppuration under it, mild antiseptics, such as boracic acid compresses, may be applied.

If, after the removal of the scab, the tissues seem thickened beneath the skin, longer applications, screening the plaque with light lead screens one or two-tenths of a millimeter in thickness, are given.

One other point to be remembered in treating rodent ulcer is that practically all observers report that where X-rays have previously been used the radium rays do not seem to exert their action so quickly and therefore healing is longer delayed. This can doubtless be explained by the fact that the X-rays, not having the selective action for the cancer cell that radium has, damage the normal as well as the pathological cells, so that proper reaction and healing do not so quickly take place.

To illustrate what results may be anticipated in this condition the reader is referred to the accompanying photographs of a case of rodent ulcer involving part of the lower eyelid and the temporomalar region. The disease had continued to increase in spite of various treatments, including X-rays. With applications of radium the ulcer soon cicatrized and the second photograph shows the result seven weeks after treatment was commenced.

Fungating epitheliomata, like rodent ulcers, offer themselves readily for radium treatment. Two methods may be used, depending on the exigencies of the case and the convenience of the patient and the physician. The case may be treated by radium alone, or a large portion of the fungating mass may be curetted and radium applied to promote the healing of the large ulcer remaining. The latter of these methods has the important advantage that considerable time is saved. The vegetations can in almost all cases be removed under a local anesthetic, and after forty-

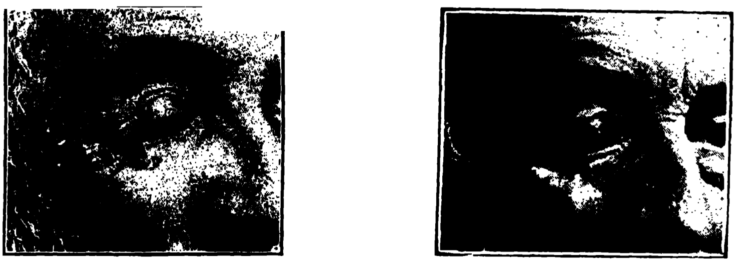

Fig. 4.

Rodent Ulcer Before Treatment. **Appearance Seven Weeks Later.**

(Author's Collection.)

eight hours the radium plaques can be applied. The dose given should be heavy so as to destroy all neoplastic cells in the base and edges of the ulcer. In cases from out of town it is better to give a very heavy dosage so that the patient will not have to return for about six weeks. When the patient can be kept under observation and seen every few days, a less severe reaction may be induced.

Using heavy filters and obtaining what Wickham calls the "surpénétrant" radiation is an excellent way of treating these cases. The diseased tissues are situated more deeply than those of the rodent ulcers, and, by using the harder penetrating Gamma rays, with long applications of fifty, one hundred, or more hours, one can act on these deep tissues without producing too much superficial destruction. The plaques may, in these cases, be left in position all night, or even day and night continuously, if convenient. The "cross-fire" method of application is often very serviceable here, as one can by this method get a very intensive action on the deeper tissues.

It is most essential, after cicatrization has been effected, that the patient should be seen every two or three months, so that any suspicious thickenings in the scar may be appropriately treated by further applications. It takes several months for the reaction to completely subside. The patients frequently complain of a sense of irritation in the scar, and there may be slight desquamation for some time. Reliable statistics give 90 per cent. of cures in the treatment of superficial cutaneous epithe-

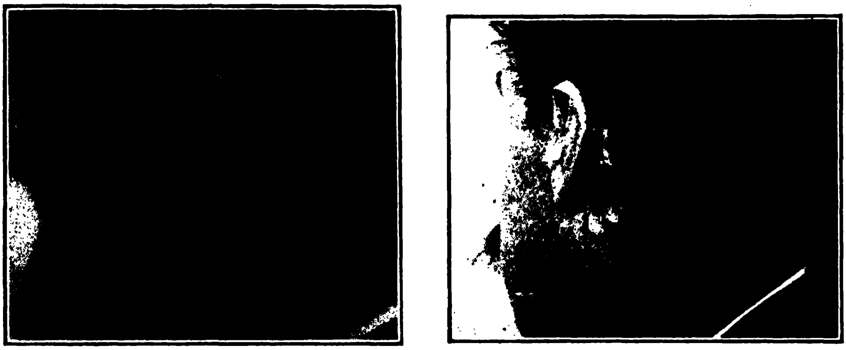

Fig. 5.

Epithelioma of Skin Before Treatment Epithelioma of Skin After Treatment.
(Author's Collection.)

liomata, and the duration of time during which there has been no recurrence extends over the seven or eight years, during which radium has been used.

Cancer of the Buccal Mucous Membrane.—These lesions must be considered in a class by themselves, for the reason that they do not react in the same way as do carcinomata of the skin, or even of other mucous membranes. Experience has taught that here all irritation should be avoided as much as possible, and that only filtered rays should be employed. Statistics are hard to obtain, but certainly results are not, as a rule, so good in the cancers of this region. Cases where there has been no recurrence for two years have been reported by Abbe, Etner, Danlos, and others.

The reasons for the less successful results in this region have been ascribed by Dr. Wickham to four causes:

1. Special sensitiveness of the mucous membrane.
2. The rapidity of invasion of the lymphatic vessels.
3. The weight of the thick filters required, which is a source of irritation.
4. The impossibility of leaving such heavy instruments in contact with these cancers for a sufficiently long time.

It has been pointed out by Gaucher that, in using the ordinary caustics, one has to use extreme caution, owing to the special sensitiveness of

the mucous membrane here, and therefore the slightest irritation from radium should be avoided. For this reason only hard Beta and Gamma rays should be employed and long exposures should be given. The difficulties in effecting this are set forth above by Wickham, and, in addition, one might add, that to secure a sufficiently heavy "surpénétrant" radiation very large quantities of radium are required. On the whole, as the radium situation is at present, the surgeon should be asked to remove as much of the neoplastic tissue as possible, and applications of radium should be made subsequently. In a great many cases where the patient refuses any procedure of a surgical nature, one is quite justified in employing radium alone, as a certain number of cases have done well under its influence only.

Cancer of the Lip.—During the early stage, when the tissues are not deeply involved and there is no induration or glandular enlargement, the writer's experience has been that radium gives good results in epithelioma of the lip. If the growth has extended so as to invade the mucous membrane of the mouth, it is well to advise surgical measures in addition to the use of radium. Best results have been obtained by treating the condition like rodent ulcer, using naked plaques for four to six hours, sufficient to produce surface reaction, and also using longer applications of screened plaques to secure deep action. Wickham and Bayet have both reported favorable results, but cases have not been a sufficient length of time under observation to give any final opinion as to the end results of treatment.

Cancer of the Tongue.—In undoubted carcinoma of this organ radium, as we employ it at present, cannot be said to be a very effective therapeutic agent, but in the treatment of certain conditions which are regarded as the precursor of malignancy it has proved effective. Such conditions are leukoplakia, and certain indolent ulcers, which are often accompanied by a history of specific disease. In leukoplakia, by using plaques so as to produce a moderately severe reaction, the normal appearance has, in a good many cases, been restored to the parts.

Cancer of the Breast.—With the exception of the local condition of the nipple known as Paget's disease operative procedures should be suggested where there are favorable indications for surgical removal. Nevertheless radium has a distinct place in the treatment of these conditions, for, in cases where either from the advanced age of the patient or from the local condition, operation is contraindicated, it has been established that radium may be of great service in the relief of pain, and even in apparently arresting the progress of the disease. Thus Wickham and Degrais report a case of a patient seventy-two years old with inoperable cancer, where the lesions have retrogressed and the patient enjoys good health. Bayet has reported cases of recurrence following operation where diminution has been obtained and the growth apparently held in check.

In such cases massive doses should be employed, properly screened to prevent skin irritation, and if masses are present radium tubes should be inserted directly into them. It is in these conditions that what may be called the prophylactic use of radium plays a very large part, as will be discussed later.

Cancer of the Uterus.—Here again, as in carcinoma of the breast, operative procedures are always to be recommended, if feasible. In non-operable cases, and as an extra safeguard against recurrence, radiation is indicated and has proved of great service. Fungating bleeding vegetations on the cervix have, by the use of plaques and tubes sufficient to cause destruction, been made to disappear, and by the lessening of the neoplastic tissues inoperable cases have been rendered operable. Foul and bloody discharges have been diminished and made to cease. The convenient form of radium apparatus allows it to be used very readily in these conditions. Tubes, for instance, can be inserted directly into the uterine canal, and small plaques may be placed directly against the cervix and held in position by a tampon. Fairly heavy doses may be given, and the writer has never, as yet, seen bad results follow even an excessively large dose. For instance, a plaque of 500,000 activity screened with two layers of rubber may be placed against vegetations in the vault of the vagina and left in place all night—twelve hours—at a time, and this can be repeated two or three times a week without producing other than beneficial results, as shown in the decrease of pain and discharge, and the healing of any raw ulcerated surfaces present. "Cross-fire" action may be obtained on the body of the uterus by having a tube in the canal and a well-screened plaque externally on the abdomen, or another tube may be inserted in the rectum.

Sarcomata.—As in the case of carcinomata certain types of sarcomata are more readily influenced by radium than others. Small, round-celled sarcomata and the myeloid form are much more amenable than tumors of the spindle-celled variety. A case of giant-celled sarcoma of the lower jaw was removed seven years ago by Abbe, and there has been no recurrence since. The same writer reports a small round-celled sarcoma of the eyelid reduced in the same way. Wickham and Degrais report several cases, some of which had recurred after operation, where further growth had been checked. Personally the writer has had the best results in small round-celled sarcoma. These are best treated, if possible, by making an incision into the mass and inserting a tube of radium, inclosed in a celluloid capsule, directly into the neoplastic tissues. This may be left in position from seventy-two to ninety-six hours, or even more. If with this one can apply plaques externally, and thus secure a "cross-fire" action, so much the better. Depending on the size of the mass other openings may be made and tubes inserted so that the growth may be attacked from all points. The result may be that a considerable necrosis is produced,

and there will be a discharge of broken-down tissue through the artificial openings for some days. Following this there is a replacement of the malignant tissues by embryonic fibrous tissue which finally leaves hard fibrous nodules in place of the neoplasm. During the necrotic process, if it occurs (as it sometimes does not), there may be some systemic reaction with a slight elevation of temperature and acceleration of the pulse rate. This need not cause any anxiety, as it usually clears up after giving some calomel and a saline. Of course the strictest antiseptic precautions must be exercised in carrying out the minor surgical procedures necessary. The use of injections of radium salts is one of the recent methods which deserves particular attention in this connection. In this way a permanent center of radioactivity can be created, and the Alpha rays which form such a large percentage of the total radiation and are lost in the other methods used can be utilized. By the use of radium ions also, as mentioned in the first portion of this article, Haret and Wickham have

FIG. 6.—SARCOMA OF THE LOWER EYELID, SHOWING CONDITION AT THE BEGINNING OF TREATMENT, AT THE END OF TWO WEEKS, AT THE END OF FOUR WEEKS, AND DISAPPEARANCE AT THE END OF EIGHT WEEKS.

(Collection of Dr. Robert Abbé.)

obtained retrogression in sarcomatous tumors. Results are as yet too recent and few to make any definite statements as to the value of this procedure, but it would seem to be a method of great service.

The action of radium on small round-celled sarcomata cannot be better depicted than in the accompanying series illustrative of a case treated by Dr. Robert Abbe, of New York. The tumor was in a middle-aged man, and had progressed for more than a year in spite of Roentgen ray treatment. Four applications of one hour each of 20 milligrams of radium bromid were made. It began to diminish in size in two weeks, and continued to retrogress until in eight weeks it was gone. There has been no recurrence, and in fact there is nothing to distinguish one eye from the other.

Malignant Disease of Other Viscera.—Experimentally radium has been used in a large number of conditions, either alone or combined with as much surgical procedure as was feasible. While the results obtained can in no sense be regarded as established we introduce some of them here

because radium therapy is as yet in its beginning, and as newer techniques develop it is altogether likely that the field of its usefulness will become more certain and more extensive.

In cancer of the *bowel,* for example, radium tubes have been brought into contact with the diseased area by means of an artificial anus, or through the operation wound. Gaultier and Labey introduced radium through the orifice left after gastroenterostomy and applied it to the pylorus, a strong well-screened plaque being at the same time applied to the abdomen, so as to secure cross-fire action. The condition of the patient improved after the treatment was commenced, and eighteen months later his general health was much better. In rectal conditions it is comparatively easy to introduce tubes, and Wickham reports a case in which a large hemorrhagic and suppurating cancerous mass was reduced to a certain extent and the hemorrhage and discharge were arrested.

In malignant disease involving the *bladder, urethra* or *prostate* cases have been reported where amelioration had been produced by the application of radium, which in this region can be inserted through the urethra or through the rectum, and thus brought into contact with the affected part.

The Position of Radium as a Therapeutic Agent

As is the fate of all new therapeutic measures, the introduction of radium was received with extreme enthusiasm on the one hand, and with ultra-conservative skepticism on the other. This was chiefly on account of the claim of the first observers that radium was an apparent means of cure of certain malignant growths. Over its many fields of usefulness in other conditions there has been little controversy, and its position as an agent of the first importance in dermatology, and in the treatment of nævi and angiomata, is well established. Its use in internal medicine is as yet too brief to allow of any arbitrary statements, but it is reasonable to suppose from results already recorded that a distinct place awaits it in the treatment of many chronic disorders. In the treatment of superficial epitheliomata it should be the method of election on account of the painlessness and simplicity of its application and the uniformly good results, many of which have extended back to the time when it was first introduced. The after cosmetic result is such as can be obtained by no other method of treatment. When one comes to malignant disease of other parts one must lean to the conservative side, and advise surgical measures where such are feasible. It is true that there are many well-authenticated cases reported where good results have been obtained in cancer of the breast, sarcomata, etc., but hardly enough as yet to warrant one in advising radium therapy alone. This does not mean that radium has no place in this connection. On the contrary, it occupies a most important place,

and one that is daily becoming more recognized as an invaluable one. This is the use of radium as a preliminary to surgery, and as a post-operative means to prevent recurrence. It has been shown by histological examination that a free use of radium plaques over such a region as the breast results in a most striking necrosis of the neoplastic cells, so that its use over the whole operation field considerably lessens the malignancy of the tissues, which are later to be cut and dissected by the operator. Following removal the tissues should be again well radiated. For this purpose a plaque screened with lead should be left *in situ* for ten or twelve hours over each point, until the whole field is covered, and this process repeated every two or three months during the first year, and slightly less often during the second and third years.

With such measures recurrence can in a large number of cases be prevented in conditions where the type of neoplasm has been such that a very grave prognosis has been given. In fact, where repeated operations have been done for two or even three recurrences, the use of radium in the way described has prevented further recurrence, which, from the previous history, might reasonably have been expected.

In non-operable conditions radium in a large percentage of cases relieves pain, lessens discharge, and may cause shrinkage of the tumor mass, so that even where a cure can not be anticipated such beneficial results warrant its use.

Finally it must be remembered that radium therapy is a very new subject, that as yet there is comparatively little radium produced, so that the quantities available are small, and that new methods of using it, such as by injections and electrolysis, are at present under investigation, and give promise of being of great service. When we have larger quantities at our disposal there is reason to hope that many conditions before which we now stand comparatively hopeless should be cured.

CHAPTER XI

X-RAY THERAPY

SIDNEY LANGE

Radiotherapy, in its broadest sense, comprises any form of radiation employed for therapeutic purposes. The X-ray is but one form of radiant energy. While the term radiotherapy has been commonly employed to signify treatment by X-rays, the term *X-ray therapy* or Roentgen therapy is the more accurate and preferable term. Although this chapter is to be confined to a consideration of Roentgen therapy, some fundamental concepts of radiant energy in general must be included.

PHYSICAL PRINCIPLES

Radiation or *radiant energy* is a form of energy produced by inconceivably rapid and regular vibrations of the imponderable substance, ether, which permeates space and matter. Depending upon the rate per second or frequency of the vibrations, various kinds of radiant energy may be differentiated. The physical properties and physiologic action of the different forms of radiations vary with their frequency and wave lengths.

These radiant energies may be classified in regular sequence, according to their frequencies. In order to give a tangible explanation of the nature and method of production of the various forms of radiations, the new conception of matter is essential. If the atom be subdivided into its ultimate component parts, units of matter or "corpuscles" (as Thompson termed them) will result. Each corpuscle has been calculated to have a mass of one seventeen-hundredth part of an hydrogen atom. It is believed that all matter can be reduced to the same ultimate unit (the corpuscle), and that the different elements vary not in essential composition, but only in the number and arrangement of the corpuscles making up the atom. Each corpuscle has a negative charge of electricity, and, although mutually repellent, they are bound together by the positive charge of the atom as a whole. According to accepted theory, the activity

of the negatively charged corpuscle (termed "electron" by Stoney) is responsible for the production of the various forms of radiant energy, and the character of this activity determines the nature of the radiant energy produced. This activity of the corpuscles is always vibratory, but varies in rate and amplitude, or simply in velocity. The production of the various forms of radiant energy and their relation to the more familiar forms of energy can be illustrated concretely in sequence by imagining a progressive acceleration of the vibrating corpuscles of any atom. When the rate reaches 75,000 millions per second, electromagnetic or electrical rays, with their attendant phenomena, result. Increasing the rate up to 160 billions, their activity would be perceived as heat rays. Executing vibrations from 400 to 790 billions per second, light rays (red to violet) would be produced, to which rays the retina is attuned. Further increase of the frequency would give rise to ultraviolet or Finsen rays, which are invisible to the human retina. Continued tremendous accelerations of the vibrating electrons would produce Hertzian rays, and finally the X-ray.

Whether the theories as outlined and implied in the foregoing considerations be accepted or not, some such concrete conception of the nature and relation of the X-ray to the physical universe is essential to a clear understanding of its method of production and physical properties. We may regard the X-rays, then, as a form of light energy differing from sunlight in having an inconceivably rapid rate of vibration and shorter wave length. Its velocity has been calculated to be practically the same as that of light (Blondlot, Marx). But its physical attributes are so unique that it stands apart as the most wonderful of radiant forces.

Production of the X-ray.—For the production of the X-ray an electric current is sent through a tube exhausted to one-millionth of an atmospheric pressure. While the phenomena accompanying the discharge of high tension currents through rarefied gases are still but imperfectly understood, the following is the generally accepted idea of the series of changes taking place:

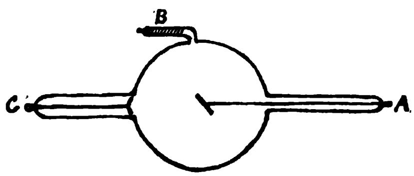

FIG. 1.

The current flows in at the anode terminal, A, and by its high potential ionizes the residual air particles in the tube. They become carriers of electricity, transferring it to the cathode or negative terminal.

The high potential at the cathode terminal, C, together with the diminished restraining pressure, causes dissociation and repulsion of negatively charged corpuscles (electrons) derived from the residual gas particles in the immediate vicinity of the cathode and from the metal of the cathode terminal itself. These corpuscles travel in straight lines from the cathode, and, meeting with comparatively little resistance, acquire a tremendous velocity. This stream of flying negatively charged corpuscles is known as the *cathode stream*. Its velocity is calculated to be one-third that of light. The stream can be deflected by a magnet, and has some penetrating powers. Wherever the cathode stream strikes a solid object, whether it be the glass walls of the tube or metal terminals within the tube, a disruptive discharge of exquisitely rapid vibrations is initiated, constituting the X-ray. Theoretically, this disruptive discharge is the result of the readjustment of the lines of electromagnetic force which surround each electron radially, and which are deflected backward by the drag of the ether, when the electron is in motion. When the moving electron suddenly loses its motion by coming in contact with a solid object within the X-ray tube, the readjustment of the deflected lines of force causes a tremor or shock to start from the electron and to run out with the velocity of light along each line as an expanding spherical shell through the ether, the thickness of which depends upon the time during which the electron is changing its motion; hence upon the initial velocity of the cathode stream and the hardness of the solid object which it strikes. Part of the energy of the cathode stream is, however, transformed into heat and fluorescence. In order to direct an intense stream of X-rays in a given direction, instead of having them scattered diffusely over the tube, the cathode terminal is made concave, causing the cathode stream to come to a focus, at which point an anode or target of heat-resisting metal is placed. At this point, the so-called focus point of the target, the chief mass of X-rays originate, and travel in all directions. This is the principle of the focus tube, as first devised by Jackson. Being able thus to control and direct the X-ray output, tubes of various shapes may be devised, making Roentgen therapy of any part or cavity of the body practicable.

Physical Characteristics of the X-ray.—Certain physical characteristics of the X-ray, which form the fundament of Roentgen therapy, must be clearly understood.

The X-rays are invisible to the human eye. The peculiar brilliance of the X-ray tube is due to the fluorescence induced in the glass. The color of the X-ray tube will depend upon the composition of the glass. Soft, or sodium, glass gives a pale, greenish-yellow color, while the hard lead glass fluoresces blue.

The X-ray travels in straight lines. It cannot be reflected, diffracted, or polarized.

The X-ray penetrates all matter approximately in inverse proportion to its density. The resistance offered by any substance to the X-ray depends upon the amount of energy abstracted from the X-ray stream by the atomic constituents of that substance. The energy is lost in imparting motion to the corpuscles of that substance. The greater the number of corpuscles in the atom, the greater the resistance offered, and the greater the number of rays absorbed. Hence, the X-ray penetration of the elements varies inversely with the atomic weight of that element, and the penetration of the compounds varies inversely with the atomic weight of their constituents. The transparency of a substance to the X-ray is entirely independent of the physical state of that substance, or the groupings of its atoms or molecules. It varies, however, inversely with the thickness, or number of layers of that substance.

Physical Effects of the X-ray.—The X-ray produces fluorescence in various materials, especially platino-barium-cyanid, calcium-tungstate, quinin, etc. The X-ray produces many chemical changes. For example, it precipitates iodin from an iodoform solution, and calomel from a solution of mercuric chlorid and ammonium oxalate. It reduces the silver bromid upon the photographic plate. The X-ray produces color changes in certain salts, platino-barium-cyanide, etc.

Every particle of matter which is penetrated by the X-rays absorbs X-rays (of varying quantity and quality), becomes radioactive, and gives off minute rays similar in character to the X-ray itself. These rays are known as *secondary rays.* They give rise to an extensive diffusion of the X-ray, an important factor to be considered in protecting the patient and operator. The X-ray is analogous to, perhaps identical with, the Gamma ray given off by radium.

GENERAL TECHNIQUE

The X-ray Tube.—The X-ray tube is, of course, the center of interest and study in the practice of Roentgen therapy. Modern X-ray tubes are of intricate design and of uncertain efficiency. While great improvements have been made in them, they are, as yet, far from perfect. The physical laws underlying the production of this powerful radiation in the vacuum tube are largely speculative, and there are still gaps in our knowledge of the cycle of events occurring in the Crooke's tube which even our theory does not bridge over. Anyone desirous of practicing efficient X-ray therapy must study the X-ray tube. In spite of the scientific uncertainty connected with its action, a good practical working knowledge may be obtained by any careful observer. Since hard and fast rules governing the manipulation of the tube cannot be laid down, it follows that a certain period of time must elapse before an operator can become

a safe X-ray therapeutist. A year or two spent in diagnostic X-ray work (radiography), where the danger to the patient is practically nil if a modern type of apparatus be used, and where abundant opportunity is offered for a thorough study of the X-ray tube in action, is perhaps the best preparation for successful X-ray therapy.

Quality and Quantity of Radiation.—The fundamental fact that X-rays are not homogeneous is the most important one in X-ray therapy. Early failures, disagreements, and lack of standardization of results in Roentgen treatment were undoubtedly due to the great variation in the quality of rays emitted from different tubes or from the same tube under varying conditions. Their range in quality is much larger than the range of the whole visible spectrum.

Quality of X-ray radiation means *penetrating power,* velocity, or length of the rays. Rays are classified as hard, medium, and soft rays. The radiation from every tube is always mixed or heterogeneous. It is, however, possible to select and regulate a tube so that one or the other type of rays will predominate. Depending upon whether the greater per cent. of rays emitted are hard, medium, or soft rays, we speak of high, medium, or low tubes.

Penetration or hardness of a tube depends upon the degree of its vacuum. As the air is exhausted from an X-ray tube, the quality of the rays constantly changes, and they become more and more penetrating. At the same time the internal resistance of the tube becomes higher—that is, the current finds more and more difficulty in passing through the tube —until finally the internal resistance reaches the point where no current at all will pass. The tube will not light up and is useless for any purpose. This observation is in harmony with the theory of the discharge of electricity through rarefied gases. The current is carried by ionized residual gas particles. If there are no residual gas particles (that is, a perfect vacuum), no current will pass. Hence, in pumping a tube, few or many residual particles may be left. If many are allowed to remain in the tube, they will carry much current; but, owing to mutual interference, the electrons of the cathode stream will not attain their greatest velocity, and the X-rays resulting from their impact on the target will be of low penetrating power, and the tube will be a soft tube. Conversely, if there be fewer residual air particles in the tube, the cathode stream can attain a greater velocity because unhampered (providing, of course, that the potential or voltage at the cathode terminal is sufficiently high), and the rays will be hard or highly penetrating rays. A small percentage of soft rays will, however, be admixed with the hard. Such a high tube will take less current, owing to its higher internal resistance. Such a conception of quality of X-radiation is a *sine qua non* of successful therapy; for, analogous to sunlight, the greatest effect of X-radiation is elicited where the ray ends or is absorbed.

Quantity of Radiation.—Intensity refers to the number of X-radiations emitted from the X-ray tube at any moment; or, more accurately, to the number of rays falling upon a unit area at any given moment. Intensity is the rate of delivery. *Quantity* is the product of the intensity and the time. If we presuppose that each electron excites one and but one ether impulse, it follows that the more residual gas in the tube (i. e., the lower the tube), the greater will be the number of X-radiations sent out, providing always that the amount (milliamperage) of current supplied to the tube is sufficient to energize each corpuscle. Although the above supposition has not been proven, the deduction works out practically. The lower the tube (within certain limits) the more current will pass, and the greater will be the intensity of the radiations produced. Analogous to optical light, the intensity of X-light varies inversely as the square of the distance from its source, and directly with the angle of incidence.

Regulation of Quality and Quantity

The technique of X-ray therapy resolves itself simply into the proper adjustment of quantity and quality to the need and nature of the affected organ or part. Accuracy in the measurement of dosage is important for two reasons:

1. The quantity and quality must be so regulated that the rays will be absorbed by the proper tissues in proper amount.
2. The patient must be protected against the dangerous results of overdose.

The factors to be considered in administering an X-ray treatment are:

1. Penetration (quality of rays).
2. Intensity (rate of delivery).
3. Time of exposure.
4. Distance of source of light from the part treated.

An inadequate application of the above factors, and an inability to accurately measure the factors one and two, have been the chief sources of past failures and burns in connection with X-ray therapy. Early operators worked more or less empirically, and their good or bad results were largely a personal matter, often accidental, depending upon the character of their equipment. While further improvements in the instruments for measuring penetration and intensity are still to be desired, the degree of accuracy now possible in determining X-ray dosage certainly equals that of other therapeutic measures, and the stigma of inaccuracy in dosage should be no longer attached to this form of therapy.

Penetration.—As previously stated, penetration depends upon the velocity of the particle of the cathode stream, and, while this velocity can be varied by varying the potential (voltage) of the current energizing the

X-ray tube, the most available method of varying the penetration is by increasing or decreasing the number of residual gas particles in the tube. Tubes may be pumped high or low during manufacture; and, when purchasing tubes for therapeutic use, a tube producing hard or soft rays may be obtained. But the vacuum of an X-ray tube is not stable. It varies with the length of time the tube has been used, and with the character of such usage. Indeed, the vacuum may vary from moment to moment during any single exposure. With continued usage over weeks or months, the vacuum of an X-ray tube tends to get higher and higher, and the rays more and more penetrating. How the gas is used up is not entirely clear. The older theory regarded the loss of the residual gas as due to the extrusion of corpuscles through the glass walls of the tube, such extrusion being supposedly essential to the production of the X-ray. The cause of this change in vacuum has more recently been explained in another way. The heavier metals making up the terminals exposed in the vacuum become vaporized with use, very slowly under ordinary usage, but more quickly when heavy currents are sent through the tube. The vaporized metal is deposited on the walls of the glass, visible in old and badly used tubes as a dark coating on the inner surface of the tube. With this deposition of metal, minute air particles are imprisoned and thus abstracted from the residual air mass. These particles have been recovered experimentally from the walls of old broken tubes. To permit of replacement of these lost particles, and thus prolong the life of the tube, as well as to provide for a rapid and convenient method of adjusting the vacuum to the nature of the application, various regulating devices are attached to tubes (Fig. 1 B). Some of them depend upon the principle of osmosis (a small palladium cylinder, when heated in an alcohol flame, allows nascent hydrogen to pass through it), but the usual type depends upon the liberation of gas from some chemical, such as K O H, by electrical dissociation or heating, or by the liberation of gas from compressed mica. By the use of such devices a high tube can always be lowered to the required degree. A low tube, however, can be raised in vacuum only by repeated use of same, the process often requiring months. But all tubes tend to become low in vacuum during any single continued exposure which lasts long enough for the tube to become hot. The change in vacuum is due to the liberation and expulsion of minute gas particles from the metal parts of the tube. Thus the character of the rays may change during an exposure, and not only defeat the purpose of the treatment, but result in injurious consequences as well. For success in therapy, therefore, it is essential not only to adjust the initial vacuum of the tube to the purpose of the treatment, but to so select and operate the tube that it will remain as nearly as possible at a constant vacuum throughout the exposure. Since the vacuum in all tubes is apt to be unstable when the tube is in operation, this is a

difficult matter. Tubes seasoned by careful use and tubes of large diameter heat more slowly than unseasoned and smaller tubes. A heavy anode which conducts the heat from the focus point and radiates it also favors stability of vacuum. For very heavy treatments it is usually necessary either to change tubes several times during an exposure, or, better, to use a tube with a water-cooled target. Such a tube, if well seasoned, may be used for hours, and still maintain a fairly constant degree of penetration.

Some accurate method of measuring penetration must be adopted. The simplest method depends upon the fact that the internal resistance of the tube is approximately proportional to the degree of its vacuum, and hence proportional to the penetrating power of the rays emitted. This resistance may be measured in inches or centimeters on a graduated parallel spark gap or spintermeter. A tube which backs up a parallel spark of from ½ to 1 inch may be considered low. A medium tube will show a parallel spark reading of 2 to 3 inches, while a high tube will back up 3½ to 5 inches. This method will be found a fairly accurate gage of the quality of the rays, although the readings vary with the quantity and voltage of the high tension current used. Furthermore, it occasionally happens that a tube becomes "cranky" and, although emitting soft rays, will give a high spintermeter reading. The spintermeter reading will likewise vary with different types of generating apparatus used, probably due to differences in voltage. However, when only one type of apparatus is employed, and when the current used is small and not subject to great variations (currents of 1 to 5 milliamperes), the spintermeter may be considered a fairly reliable guide.

More accurate instruments which measure the penetrating power of the ray directly may be used. Walter's penetrometer consists of a sheet of lead with 8 windows covered with platinum of varying thickness, and over which a small fluorescent screen is placed. The penetrating power of the ray is gaged by the number of windows seen on the screen. Wehnelt's and Benoist's instruments consist of a standard disk and screen, the illumination of which is compared with the illumination of a similar screen through varying thicknesses of aluminium. All of these direct methods necessitate some exposure of the operator to the ray, although with the modified Benoist it is not necessary to get in the axis of the ray. Any of these instruments may be so altered, however, that the readings may be made from the operator's protected booth, by decreasing the thickness of the disks to allow for the increased distance from the X-ray tube. With the small quantity of current ordinarily used for treatment, however, the above method is not entirely satisfactory. More recently an instrument for measuring penetration in terms of voltage at the tube terminals has been devised. The penetrating power of the rays emitted are approximately proportional (within certain limits) to the voltage at

the tube terminals. The instrument which has been termed a qualimeter reads the voltage at the cathode terminal by the degree of repulsion of the leaves of an electroscope. It is to be emphasized finally that all of these methods measure the penetration of the major portion of the rays generated at the time, and that the proportion of softer and harder rays admixed is uncertain.

Intensity.—For measuring the quantity of rays emitted from the X-ray tube, two methods are available. One is the indirect method, and measures the current passing through the tube as an index of the amount of X-rays generated. The amount of current traversing the tube multiplied by the time of exposure gives the total quantity delivered. The other method, the so-called direct method, measures the total quantity of rays emanating from the tube during a given period of time by the physical or chemical changes produced by the ray in certain substances placed in its path.

For measuring intensity or rate of delivery of the rays the milliamperemeter in series with the tube is the usual method. It is generally believed that the quantity of X-rays emitted at a given moment is approximately proportional to the amount of current passing through the tube, and, when operating the tube according to the recognized rules of technique, a milliampere reading taken in conjunction with the time and the penetration may be regarded as a safe and practical method of dosage. It must always be remembered, however, that all of the electrical energy sent through the milliampere meter is not converted into X-ray energy. Some of it leaks off the wires, some is converted into heat within the tube, etc. Furthermore, it is not proven that each electron gives rise to one and but one X-ray impulse, and that the current conduction through the tube is carried on exclusively by electrons. When using an induction coil as a source of electrical energy all inverse current must be carefully cut out by the use of suitable valve tubes, as inverse current gives false milliampere readings. The number of interruptions in the primary current likewise seriously affects the reading. It has been recently shown that slow interruptions of a mercury break with an induction coil give 25 to 35 per cent. lower readings than the more rapid interruptions (110 per second) of a transformer. In other words, 2 M.A. of current from an induction coil with mercury break produce 25 to 30 per cent. more X-rays than 2 M.A. from a transformer. Furthermore, the thickness of the glass walls of the tube, which must vary with each type of tube or with each tube of the same type, influences markedly the intensity. Very thick tubes absorb a considerable percentage of the X-rays generated within. In employing the milliamperemeter to estimate dosage it must always be remembered that the work done by the X-ray analogous to work done by any other form of energy is always the product of velocity $\times$ mass or penetration $\times$ quantity, and that the penetration must always

be taken in conjunction with the milliampere reading; otherwise the latter is worthless and misleading.

The direct methods of measuring quantity are, on the whole, more accurate, although more difficult to carry out. They also approach more closely the long cherished ideal of radiologists, namely, a standardization of X-ray dosage. Since results, as computed by a direct method, can be better duplicated by different workers in different parts of the world, the adoption of such a direct method is better suited to the recording of results in medical literature. The most widely accepted direct method depends upon the fact that the X-ray produces color changes in certain chemicals. Holzknecht in 1902 introduced this method, using potassium sulphate as the reagent. At present platino-barium-cyanid has proven to be the most reliable for this purpose.

Two instruments utilizing platino-barium-cyanide have been tested and accepted by some radiologists as tentative standards of measurement. The Sabouread et Noire chromoradiometer consists of pastilles of platino-barium-cyanid and a chart containing the standard colors for comparison. Tint A (a pale green) represents the color of the fresh unchanged pastille. Tint B, which is a dark orange tint, represents the color produced by an amount of X-rays just sufficient to cause a slight erythema of the skin. Holzknecht's radiometer is a modification of Sabouread's, and consists of a delicate color scale with which the pastilles may be compared. Whereas the Sabouread and Noire instrument allowed of a reading in but one large unit, namely, the "erythema dose," Holzknecht's instrument, by means of its delicate color scale, allows of reading in units 1/5 of the erythema dose. Five Holzknecht's units or 5 H equal the Tint B or "erythema dose" of Sabouread et Noire.

The instruments are utilized as follows: A fresh unchanged pastille is placed in the central axis of the X-ray one-half the distance from the target to the skin. This rule as to location of the pastille is a purely arbitrary one. The exposure is then made, and, from time to time, this pastille is removed to another room and compared either with tint B of Sabouread's chart, or with the Holzknecht scale, until the color changes to the tint, indicating that the desired dose has been given. The comparison with tint B of Sabouread's scale is to be made in a dimly lighted room, while Holzknecht stipulates that an incandescent light should be used in matching the colors of his scale. The method of measuring dosage by the chromoradiometer has certain inherent objections. The personal equation enters in matching colors. The reagent used is not stable, and tends to change color in sunlight and hot and dry atmospheres. Furthermore, the reagent, as manufactured by different firms, is not of uniform sensitiveness, and even varies from time to time when made by the same firm. Holzknecht's scale provides for variations in the sensitiveness of the salt, and all pastilles for his instrument are tested by the manufacturer

and classified as to sensitiveness. This method is most accurate with tubes of medium hardness.

As mentioned above, the standard of comparison is the color change produced in the platino-barium-cyanid by a volume of X-rays sufficient to produce the mildest reaction in the human skin, with alopecia on the hairy regions, and nothing more. This amount, called the "erythema dose," has been determined by prolonged observation and experiment. This standard is not necessarily an inaccurate one or a flaw in the method. Since the nature and proper control of the X-rays have become better understood, it has been shown that the X-ray may be handled as any other form of energy, and equal amounts may be confidently expected to produce equal results. A danger, however, not to be underestimated in using Saboureaud's pastilles lies in the fact that, in giving such a large dose as to produce an erythema in one treatment, we are working near the danger line, and a slight error in technique may result in an overdose with its consequences.

Other methods of measuring the dosage have been advanced from time to time. As most of them have either fallen into disuse or have been relegated to experimental laboratories, their mention in such a brief treatise as this would be out of place. Some depend upon the fact that the X-ray causes chemical changes in certain solutions and throws down a precipitate which may be measured. Another method gages the volume of X-rays by the degree of ionization of an exposed gas. Since the degree of ionization varies with the quality or penetration of the ray, this method has the same inherent objection as the use of the milliamperemeter, and is, therefore, not an accurate *direct* method, although variations in the penetration of the rays affect, in a measure, the accuracy of the chromoradiometric methods also. Kienbock's quantimeter gages the ray by its effect upon strips of photographic sensitive film, using the amount of blackening produced by the erythema dose as the standard.

Notwithstanding certain weaknesses in the chromoradiometric method, the instruments of Saboureaud and Noire and of Holzknecht will, in proper hands, serve as a safe and reliable measure of dosage. Perhaps the safest plan in the estimation of dosage is to take cognizance of *all* factors, as recommended by Schmidt. While it is true that the milliamperemeter measures only the current supplied to the tube, and does not record the efficiency of the tube as a transformer, and that the penetrometers and the chromoradiometers, depending on visual estimates, must involve the personal equation, yet, if we take *all* of these factors into consideration, the determination of dosage will be sufficiently accurate.

For those who do not adopt any of the direct methods of measuring the output of the tube, and who rely upon the milliamperemeter and the associated factors to determine the dosage, some tables prepared by Walter

may be of much assistance. Walter made a large series of experiments to determine the erythema dose in terms of milliampere minutes. The factors which he had to consider in such a determination were: target-skin distance, penetration of tube, and, what has been shown to be of very great importance, the thickness of the glass wall of the tube opposite the target. By exposing many Sabouraud tablets to tubes of different penetration until the tint B (erythema dose) was produced, and taking into consideration the coefficient of absorption of glass, he developed a formula which would combine the factors of distance, penetration, and thickness of the tube in terms of milliampere minutes. Referring to his table, a tube, whose wall opposite the target is 0.6 mm. thick and which emits Walter 5 rays, will at a target-skin distance of 20 cm. deliver the erythema dose in 29 milliampere minutes. To utilize such a table, the manufacturer must furnish with each tube the measurement of the thickness of the glass wall opposite the target.

Time of Exposure.—The measurement of the time of exposure is essential in estimating dosage, if the milliamperemeter readings are relied upon. For accurate timing, and as a safeguard against overdose, a clock with an automatic time switch should be placed in the primary circuit. The clock may be set for the desired number of minutes, and the operator is free to leave the room and attend to other work, avoiding unnecessary exposure to the X-ray as well.

Two methods of administering the requisite dosage may be employed: either the entire dose may be given in one or two heavy exposures, or the exposures may be light and repeated at frequent intervals until the desired effect is obtained. In choosing between these two methods many factors must be considered, for each has its advantages and disadvantages. On the Continent, and, to a certain extent, in England, single heavy exposures are much employed; whereas, in this country the oft-repeated small exposures are usually preferred. The success of either must depend upon the operator and the character of his apparatus. If a single heavy exposure is given, the dose must be carefully measured by a chromoradiometer, which implies much experience in the use of the instrument. This so-called "massive-dose" method is especially adapted to the treatment of superficial conditions, such as skin cancer, where the desired effect, i. e., the destruction of a certain amount of tissue, can be accurately estimated. Much time is saved, and, if the operator has mastered all the details of technique, the brilliant and prompt results of the "massive-dose" method impress one with the possible accuracy of Roentgen therapy.

Much may be said, however, in favor of the small oft-repeated or "fractional-dose" method. Its safety commends it above all else. Furthermore, there is a so-called "latent" period between the application of the dose and the appearance of the maximum effect, a period which varies

from 7 to 14 days. Where the object of the treatment is not to destroy a certain amount of tissue, but, for example, to influence an enlarged gland beneath the skin, the total quantity of irradiation required is uncertain, and the effect of a small amount must be carefully watched before giving more. And where, for instance, the change produced by the ray is a slow one, and must extend over months, as, for instance, in leukemia, the single heavy dose is, of course, not applicable. Furthermore, the destruction of tissue by irradiation, whether it be a large cancerous mass (as in treating inoperable cancer) or white blood cells (as in leukemia), produces an intoxication which, in the debilitated and the aged, may be of serious consequence. Hence, it is best to proceed slowly with the tissue destruction. It is, however, true that much inefficient work has been due to the fact that the exposures were too light. Such conservatism may be the result of failure to appreciate the principles of technique, but more often it is due to the fear of producing a burn. Much of the promiscuous X-ray therapy has been of this type, and is necessarily fruitless. The inefficiency and even harmfulness of underdosing in X-ray therapy are readily explained upon considering the physiological action of the ray upon the cells of the body. Analogous to many forms of internal medication, small doses stimulate and large doses inhibit and then destroy. In treating a superficial growth or a deeper inoperable malignant condition, very small doses will not only fail to produce the desired results, but may even do harm by stimulating the cells to increased activity. A homely example may be cited in the amount of energy required to drive a nail. Small repeated blows from a tack-hammer will never accomplish the results of one or two blows from a sledge-hammer, although the total amount of work done in each case may be the same. The stimulating effect of the X-ray is often desired, however, as in chronic eczema, and a very small dose may be all that is required. But more frequently it is necessary to produce a mild inflammatory reaction (X-ray erythema) to bring about results, as in the exuberant skin lesions. In such obstinate lesions as lupus, etc., reaction after reaction must be produced. The X-ray exposures must be pushed fearlessly, yet continuously, to the desired effect, and the operator must have confidence in the accuracy of his technique. The beginner must, of course, proceed conservatively, for inefficient treatment is always to be preferred to the suffering and uncertainty incident to an X-ray burn.

In using the milliamperemeter as the gage of dosage, the time of each treatment will vary from 5 to 15 minutes, and the current traversing the tube will vary from 1 to 5 milliamperes. When the platino-barium-cyanid pastilles are used the time will vary with the intensity of the X-light employed. Very recently Albers-Schönberg introduced what has been termed "second-therapy," where the time of exposure has been reduced to a few seconds, instead of minutes. By using a transformer

delivering 30 to 40 milliamperes, an exposure of 30 seconds (900 to 1,200 milliampere seconds) would deliver the same quantity of rays as would be delivered by a current of one milliampere over 15 to 20 minutes. He has, for example, given the erythema dose in 15 seconds. Such short exposures with heavy currents give less latitude for technical errors and greatly increase the percentage of such errors.

Distance of Source of Light.—The distance of the source of the X-rays from the part being treated is of great importance, for the intensity of the X-rays varies inversely as the square of the distance. Since the X-rays originate at the target of the tube, all measurements must be estimated from the target and not from the glass wall of the tube. The adjustment of the distance must consider the location of the tissue to be treated. If superficial, the distance from the target to the lesion should be comparatively short, and a moderately soft tube used. In this way the shorter and more active rays will just reach skin where they will be absorbed, and the rays will be utilized while their intensity is comparatively great. If a deep tissue (that is, a tissue beneath the skin) is to be irradiated, a higher tube giving out more penetrating rays should be employed, and the target-skin distance should be increased. The rays, in order to reach the deeper tissues, must, of course, pass through the skin. The task of giving effective doses to the deeper tissues without injuring the skin has brought up several interesting problems. It follows from the law of intensity that more rays will always fall on the skin than will reach the deeper tissues, but the *difference* is minimized if we increase the target-skin distance. At the same time that the difference in intensity of the X-rays reaching the skin and the deeper tissues is minimized, many of the shorter, softer rays which would be absorbed by and actively influence the skin are lost in the space intervening between the tube and the body. Since the intensity falls rapidly with the increase of distance, the time of exposure must be increased to deliver an efficient dose to the deeper tissues.

Uniformity.—The fact that the X-ray will penetrate the skin and affect a deep lesion without producing any visible reaction in the skin is one of the best proofs of the existence of the most important and unique attributes of the X-ray, namely, a selective action. In order, however, to favor this selective action the irradiation of the two kinds of tissues should be as *uniform* as possible. If, for example, the lesion, which is radiosensitive, be superficially located, the central axis of the rays should be directed to the center of the lesion. If the lesion is small, the irradiation will be fairly uniform while the healthy skin at the margins of the lesion will receive a slightly less intense dose. If the lesion is large and the surface flat, there may be an inequality of intensity in different parts. In such a case it is perhaps better to divide the surface to be exposed into several parts, and expose each part separately, covering the rest with

lead foil. Unless this division and protection of the areas during the several exposures be accurate, there may be overlapping of edges of the successively irradiated areas with consequent overdose. Theoretically, only such concave surfaces as the axilla or back of the knee can be uniformly irradiated. Where the surface is convex the inequality of irradiation is, of course, greatly accentuated.

Technique of Deep Therapy

The efficient irradiation of deeper tissues, that is, tissue beneath the skin, presents many difficulties. That the rays penetrate any and all tissue in the human body is proven. But, because of the rapid diminution in intensity due to absorption as the rays traverse the tissues, the deeper tissues can receive but a small percentage of the rays falling on the surface of the body. Compared to this tremendous loss by absorption, the slight diminution in intensity as a result of the increased distance of the deeper lying tissues from the target is insignificant. This absorption varies directly with the density of the irradiated tissues and inversely with the penetrating power or velocity of the rays. It has been estimated that with a medium hard tube only 50 to 60 per cent. of the rays reach 1 cm. below the surface of the body, at a depth of 2 cm. only 35 to 45 per cent., and at 3 cm. the intensity falls to 20 to 30 per cent. The nearer the tube to the irradiated part the greater will be the percentage of decrease in intensity in the deeper tissues. Conversely, the greater the target-skin distance the smaller will be the percentage of loss from absorption by the superficial tissues.

In administering the efficient dose to the deeper tissues, the skin may be protected in two ways: The excess received by the skin over the amount received by the deeper tissues can be minimized by increasing the target-skin distance. It is rarely advisable to increase the target-skin distance over 15 inches, as the loss in intensity necessitates such an increase in the milliamperage or in the time of exposure, or both, that special apparatus and special tubes would be required. The skin may be further protected by treating, wherever possible, from different sides or different angles, so that the same skin area will not be exposed so frequently. Thus, in treating a mediastinal tumor, the exposures may be alternated over anterior and posterior surfaces of the chest. In treating the blood mass, as in leukemia, various parts of the body may be exposed successively.

The X-ray Filter.—Utilizing certain laws of absorption of X-rays, a method has been advanced which offers almost complete protection to the skin during deep exposures. It was shown by Walter that those metals near the center of the scale of atomic weights, such as silver and zinc, absorb chiefly the hard rays, whereas the metals at the extremes of the

scale, such as aluminium and copper, absorb the soft rays. In other words, if the rays are passed through silver they are for the most part soft; whereas, if they pass through aluminium, they are chiefly hard. Perthes first applied this principle to X-ray therapy on the Continent. He filtered the rays through a sheet of aluminium 1 mm. thick, thus removing most of the very soft rays. In this country Pfahler introduced the use of a piece of thick leather with the same object in view. It is a proven law of absorption that the second layer of any specified substance absorbs a smaller percentage of the rays than the first layer. Indeed, the second layer of any substance absorbs only a small fraction of what the first layer absorbs. Hence, if a piece of leather (1 cm. thick) be previously soaked in water, to make it more nearly analogous to the human skin in density, it will absorb the same character of ray as the skin would absorb. Hence, if the wet leather be interposed between the skin and the target, the majority of the rays absorbable by the skin will have been removed, while the skin, having approximately the same coefficient of absorption as wet leather, will absorb only a fraction of what passes through the leather.

The discovery of the "X-ray filter" is a most valuable addition to the technique of Roentgen therapy. By its consistent use accidental X-ray dermatitis should be a terror of the past. Even the beginner may take confidence and irradiate safely. But the expert also derives added assurance, and is relieved of much worry by employment of the filter. The amount of exposure to X-rays filtered through aluminium or leather which the skin will withstand is, in the light of previous disastrous experiences, almost incredible. This possession has enabled us to practically guarantee our patients against burns, and it has facilitated certain experimental work which, without the filter, would have been contraindicated. By its use leukemic patients may be treated for years without injury to the skin, and the hairy parts of the body may be irradiated for therapeutic or diagnostic purposes.

The filter consists of simply a sheet of aluminium 1 mm. thick, or a thick piece of wet leather. More convenient, and perhaps safest, is a thinner piece of leather glued to a sheet of aluminium. It is hardly necessary to mention that with the filter the time of exposure must be increased if superficial lesions are being treated. In deep therapy the use of the filter does not lessen the intensity of the penetrating rays. While indicated particularly in deep therapy, it finds an important place in superficial therapy as well. For instance, in treating scattered patches of psoriasis with healthy skin intervening, such a filter is indispensable. In treating epithelioma, it is usually essential to expose an appreciable margin of apparently healthy skin surrounding the lesion, which may be protected by the filter. Where it is desired to limit the degree of reaction, or to safeguard against excessive reaction, the filter is invaluable.

Other substances having coefficient of absorption similar to that of

the normal skin have been used. Besides leather and aluminium, a piece of ordinary window glass $1\frac{1}{2}$ mm. thick is perhaps the most acceptable.

Uniformity of Deep Irradiation.—To secure uniformity of deep irradiation new difficulties arise. The object of securing uniformity is to facilitate the selective action of the X-ray. Thus, if an area containing both normal resistant cells and abnormal or radiosensitive cells be uniformly irradiated, the less resistant cells will degenerate without any change in the normal cells. That there is tremendous loss of intensity in deep therapy, due to increased distance as well as to absorption, has been previously discussed. The fact that this loss is progressive and varies with each millimeter of tissue penetrated renders the deep irradiation not uniform. The desired uniform irradiation has been termed *homogeneous irradiation* by Dessauer, who considers it absolutely essential for successful deep therapy. The advantages of homogeneous exposures apply with equal force to superficial therapy. Since in superficial therapy we are dealing for the most part with lesions having flat surfaces, and whose thickness is often inappreciable, the requirements for homogeneity, such as distance and absorption, can be more nearly approached. As a general rule, the target-skin distance for superficial lesions may be established as twice the greatest diameter of the lesion under treatment (Holzknecht). To secure homogeneity in deep work, or approximate homogeneity, since theoretically absolute homogeneity is impossible, we can modify our technique in two ways. When the target-skin distance becomes so great that the thickness of the part under treatment becomes negligible, the percentage loss in intensity becomes negligible, and the irradiation becomes homogeneous. Holzknecht, therefore, places the tube 3 to 6 feet from the skin, while Dessauer recommends a target-skin distance of 20 feet, his tube being attached to the ceiling. With this increase in target-skin distance the increase in penetration must go hand in hand, so that the percentage loss by absorption will be negligible. The tube, therefore, must be excessively hard (Walter—8 or more). Such a method is mechanically inexpedient, and implies a tremendous waste of energy. Owing to the high penetration the absorption by the various tissues may be approximately uniform, but the quantity absorbed is extremely small. Similarly the great target-skin distance reduces the intensity to a small fraction of the output of the tube. To overbalance these losses, the time must be measured in hours instead of minutes. Thus Dessauer reports exposures of 6 to 8 hours daily until the total has reached 100 to 250 hours. Such prolonged exposures demand special tubes, and a special apparatus whose current is less heating to the tube than the usual type of current. Furthermore, a multiplication of apparatus and treatment rooms would be necessary, such as could only be obtained in a large, well-endowed institute.

Requirements for Deep Therapy.—Dessauer's modification of deep

therapy has not justified the claims made for it, and for the present the requirements of deep irradiation may, in a measure, be fulfilled without resorting to such extremes.

The practical requirements for deep therapy may be tabulated as follows:

1. Increasing the penetration of the tube.
2. Use of filters.
3. Increasing of target-skin distance.
4. Exposures from different sides.

In estimating deep dosage the pastilles must be placed *under* the filter and the amount is to be always kept below the erythema dose.

Protection of Patient and Operator

Of great importance in X-ray therapy is the *protection* of all parts of the patient's body not under treatment, as well as the protection of the operator and his assistants, from any unnecessary exposure. The disasters from overexposure and unnecessary exposures occurring early in the Roentgen era have so firmly impressed upon all workers the necessity of certain protective precautions, that the practical methods of safeguarding against injury are generally understood. With the recognition of the possible danger from excessive exposure came a wave of excessive apprehension in the use of the X-ray. Some operators were so alarmed as to give up the work entirely. In the matter of protection, we should avoid extremes in either direction. Unnecessary exposure of either operator or patient to the X-ray is unwarranted; but absolute protection from all irradiation is not always attainable.

For the protection of the patient he may be covered with some more or less ray-proof material. Most convenient and available is lead foil. It has been found that lead foil 0.25 mm. thick absorbs practically 96 per cent. of the rays of the character ordinarily employed for therapy, and the 4 per cent. which passes through cannot possibly injure the skin. Thus, in administering a dose of 10 H., or twice the erythema dose, the skin covered by the protective foil will receive but ½ H. As it requires at least 3 H. to produce the very mildest reaction, the protection thus afforded is ample. The lead foil is easily wrinkled and torn unless covered with cloth or rubber and bound around edges. Furthermore, it is apt to become soiled and unsanitary. It is much preferable to inclose the tube in a ray-proof shield or box, and allow a bundle of rays to emerge through an opening which may be adjusted to the size of the lesion under treatment. A single sheet of lead foil may then be employed to cover the healthy skin around the margins of the area under treatment. To avoid a possible carrying of infection, each patient should have his own sheet

of foil, which may be preserved unwrinkled and separate from the rest by filing it alphabetically in an ordinary letter file.

Inclosing the tube in a ray-proof receptacle is the only scientific method of controlling the rays. The use of an "open" or uninclosed tube cannot be too strongly condemned. The inclosed tube protects not only the patient, but the operator and all others in the room as well. The container for the tube may be a lead-lined box, or, in order to obviate the sparking which is almost inevitable where so much metal is in close proximity to the tube, a ray-proof rubber cloth may be used to make the receptacle ray-proof. Rubber cloth can now be obtained which has a high coefficient of absorption. Because of its cleanliness and flexibility, it is often preferable to the lead foil as a covering material, and may be put to varied uses in connection with X-ray therapy. The best container for the tube is the heavy shield made of lead glass which is practically opaque even to the most penetrating ray. These shields have the added advantage of permitting constant observation of the tube during operation. They are open above, however, and allow a certain amount of stray radiation to escape in the room. It should be understood that the danger lies in the path of the direct rays from the active hemisphere of the tube. Therefore, the active hemisphere should always be turned away from the operator. The stray radiation from the inactive or dark hemisphere, viz., the half of the tube behind the target, cannot be regarded as necessarily dangerous. The entire atmosphere of any room of ordinary size in which an X-ray tube is being operated becomes radioactive even though the tube is inclosed in a glass shield. The operator and assistants in such a room will be bathed in this secondary radiation. It has never been proven that such secondary radiation is positively injurious. Albers-Schönberg recently exposed guinea-pigs for 3 months to such secondary radiation and found no demonstrable effect upon them. However, the generally approved procedure for the operator is to avoid even such secondary irradiation. He may, therefore, either enter a lead-lined booth (lead 1/16 inch thick) or leave the room. The switchboards should be located in such a booth or in an adjoining room; and, by means of a lead glass window, the tube and the patient may be kept under constant observation. Unless the partition between the rooms be brick, it should be reinforced with sheet lead 1/16 inch, or it may be built double and filled in with sand. In order to observe the tube indirectly a mirror may be conveniently arranged. For the extremely cautious ray-proof gloves, aprons, and glasses have been provided. The folly of exposing the hands to test the tube or any part of the body unnecessarily need hardly be mentioned.

BIOLOGICAL EFFECTS OF THE X-RAY

The biological action of the X-ray must be clearly understood in order to permit of the rational use of the ray in therapy. X-ray therapy is no longer empirical, but is based upon a fairly well-developed pathology. When the nature of the ray and its action upon the human tissues are generally known, the X-ray can take its place in our therapeutic armamentarium to be employed not as an experiment or as a method of last resort, but as a routine therapeutic agent whenever the indications arise.

The X-ray acts not by "burning," as was formerly popularly supposed, but by a unique action upon the molecular, atomic, or subatomic structure of the tissues. Such effect upon the structure of the complex protoplasmic molecules gives rise to altered metabolism, altered function, or tissue degeneration and destruction. The results may be recognized clinically as stimulation, irritation, or loss of tissue. All cells which have absorbed X-light suffer a chemical change which may produce no appreciable effect, or may result in stimulation, irritation, or degeneration. The effect upon the tissue will depend upon:

1. The amount of rays absorbed by the tissues.
2. The selective action of the ray.

The treatment may be given only to stimulate, as in chronic eczema and indolent ulcers; or to produce a mild inflammatory reaction, as in chronic infections of the skin; or to inhibit functions, as in hyperidrosis or pruritus; or it may be pushed to produce actual destruction, as in carcinoma. Again, its indirect action may be sought, as in sycosis, where the tissues are stimulated to produce an antitoxin to combat the bacteria, or in treating enlarged tuberculous glands where, in addition to the possible destruction of diseased lymphoid tissue, the cells are stimulated to fight the bacilli. The lesion to be subjected to X-ray therapy must be accurately diagnosed and the desired result determined upon. Then the X-ray dosage may be varied to bring about the effect desired. The therapy should never be given in a hit or miss way, even in experimental work, but definite Roentgen effects should be planned.

The characteristic and unique curative action of the X-ray is the production of a cell degeneration which can be demonstrated microscopically. The action is purely local and, contrary to external or even internal medication, it reaches every cell in the irradiated area. Any general effects which may follow X-ray exposures are due either to serological changes in the blood, e. g., the development of leukolysins in leukemia, or to the toxemia which may accompany the tissue destruction.

An inflammatory reaction often accompanies the X-ray action proper, but the X-ray curative effect is not in any sense inflammatory. The inflammatory reaction, however, often aids the X-ray action proper. Such

an inflammatory reaction is, of course, essential in the repair of tissues following destructive irradiation.

Selective Properties of X-rays,—The selective property of X-rays is the basis of Roentgen therapy. The normal tissues of the human body may be classified according to their sensitiveness or susceptibility to the influence of irradiation. The tissues may be said to possess varying degrees of sensitiveness to the X-ray. Those which react to the X-ray not at all or only after the severest irradiation are said to be resistant, while those tissues which are more easily influenced are said to be radiosensitive. If an area be irradiated uniformly, the resultant change in the cells of that area will vary greatly, depending upon the radiosensitiveness of the different types of cells. The presence of a pathological process in a tissue usually increases the sensitiveness of that tissue; hence, as a general rule, diseased cells and tissues may be said to be more sensitive to irradiation than healthy cells and tissues. The presence in a tissue of a simple inflammation seems to sensitize the tissue to the X-ray. Abnormal cell elements and tissues are especially susceptible to irradiation. Each pathological type of cell varies in susceptibility and may be classified in terms of radiosensitiveness. In a general way it may be said that the sensitiveness to irradiation is most marked in those cells which are rich in protoplasm and in which metabolism is active. The blood supply of the tissue at the time of irradiation likewise influences its radiosensitiveness. Anemic tissues are less susceptible than hyperemic tissues, probably because the metabolism in anemic tissues is decreased. In healthy tissues the cells which are highly specialized are influenced first. As examples may be mentioned the atrophy of hair follicles and sweat glands which occurs in the healthy skin before the exposure is sufficient to cause a dermatitis. Pathological tissues composed of young, rapidly growing cells of low vitality offer little resistance to the ray. Selective action increases as the abnormal cells approach the embryonal type. The lymphoid tissues are very susceptible, as evidenced especially in the reduction of enlarged lymphatic glands, enlarged thymus, and the white elements of the leukemic blood. Of pathologic tissue the sarcomata, whose cells are typically embryonal, are very sensitive to X-radiation. Cells which have become differentiated and entered into the structure of tissues or organs gain in resistance. Thus the round-celled infiltration of a gumma is easily destroyed, while the resulting dense scar of a healed gumma is affected with difficulty.

As a guide in the apportionment of dosage to the various lesions in various parts of the body, and as an index of the results to be expected, the following tables will be of value. The tissues are listed in the order of susceptibility to roentgenization.

Normal Tissues.—Lymphatic tissues, bone marrow, testicles, ovaries, cartilage of the newborn, skin of face of child, mucous membranes, sweat

and sebaceous glands, skin of buttocks of child, intima of blood vessels, skin of adult's face, hair papillæ, skin of buttocks of adult, liver and kidney parenchyma, connective tissue and blood vessels, muscle, cartilage, cornea, sclera, bone.

Pathological Tissues.—Leukemic and pseudoleukemic tissues, certain sarcomata, especially lymphosarcoma, mycosis fungoides, psoriasis (fresh), inflamed skin, epithelioma, acne, favus, herpes tonsurans, lupus, sycosis, certain eczemas, carcinoma, tuberculous glands, lipoma, myoma, fibroma.

The explanation of the peculiar selective action of the X-ray is not clear. The difference in density between the various tissues, healthy and diseased, is hardly sufficient to explain the great variation in the changes elicited. Schultz, however, has shown that such variations in specific gravity as .01 will cause sufficient variations in the absorption coefficient to be demonstrated upon the photographic plate. If the selective action depended entirely on specific gravity, deeper tissues, having a specific gravity greater than the skin, could be successfully treated through the skin without injury to the latter. Such a radiosensitive organ as the spleen has, for instance, a specific gravity two hundredths (.02) of a per cent. lower than that of the skin. The ovary at puberty, on the other hand, has a specific gravity of .02 higher than the skin. Until the factors of the absorptive power of the tissues are understood, the selective property of the ray cannot be predetermined. The true explanation is probably to be sought for in the varying atomic or subatomic makeup of the tissues.

While we can in a measure control and reinforce the selective action especially by varying the penetrating power of the ray, attempts have been made to directly sensitize the tissue under treatment to the X-ray. Radiosensitive drugs, such as eosin, fluorescin, which fluoresce under the influence of the ray, have been tried, with uncertain results. Schmidt has recently shown that hyperemic tissues gain in sensitiveness. In treating deep lesions, and it is chiefly in deep therapy that the necessity for such increased susceptibility exists, he induces hyperemia in the tissues under treatment by the application of the high frequency current before irradiation. He applies the method to superficial tissues, also inducing hyperemia in them by exposure to an incandescent or mercury vapor lamp. It would thus seem to follow that radiosensitiveness and absorptive power of tissues are not entirely synonymous. The coefficient of absorption of a tissue is but one factor in the determination of its radiosensitiveness. The other factor is the inherent character of the cell itself. Since we cannot influence the latter factor, we must favor the selective action of the X-ray by utilizing the former.

The secret of efficient therapy is to supply to the cell under treatment the kind of rays which it can best absorb. It is of such vital importance

and so often neglected that some concrete proof of the varying therapeutic action of X-rays of varying velocities will be given. If a superficial tumor has a low specific gravity, repeated heavy doses from a hard tube Walter 7-8 may not influence it at all, whereas a few treatments from a low one (2-3 Walter) may accomplish the desired result. Other things being equal, the softer the rays the more will be absorbed. But soft rays have comparatively little penetrating power. Hence, unless the tumor be thin, the rays will not reach its deeper parts. The percentage of the superficial intensity which reaches 1 cm. beneath the surface of water when tubes of different degrees of hardness are used is shown in the following table:

Walter—3	33 per cent.
4	40 per cent.
5	50 per cent.
6	60 per cent.

As a general rule, it may be said that, in order to facilitate absorption, the rays should be as soft as is consistent with thorough penetration and safety to overlying tissues, unless it is attempted to give "homogeneous irradiation" (the theory of which is not widely accepted); in which case the hardest possible rays are employed.

The Latent Period.—The action of the X-ray upon living tissues is characterized by a certain lapse of time between the exposure and the appearance of demonstrable tissue changes. This time, which elapses between the irradiation and the demonstrable change, is known as the "latent period." The latent period varies from a few days to three weeks. The first skin change evident after efficient irradiation is termed an "X-ray reaction." The term reaction usually refers to changes in the skin, but may be properly applied to deep changes as well. In a general way, it may be said that the latent period bears a direct relation to the amount of X-rays absorbed. The greater the amount of X-rays absorbed the shorter the latent period, and vice versa. Furthermore, the degree or type of reaction is inversely proportional to the latent period, and, of course, directly proportional to the amount of X-rays absorbed. The "latent period," therefore, is a most important consideration in Roentgen therapy, and the length of the period is of prognostic moment as to the severity of reaction which is to follow. The generally accepted fractional-dose method of therapy distributes the dose over a period of time which equals or exceeds the latent period, and the time of the appearance can be continuously watched for and the dosage graduated accordingly. The typical reaction consists of an erythema which lasts a variable length of time—a few days to several weeks—and disappears, leaving some pigmentation. Severer grades of reaction may go on to an X-ray burn. A visible skin reaction is always to be avoided, if possible, in deep therapy,

but is often essential to the success of superficial irradiation. A vigorous reaction during a course of deep treatments may necessitate cessation of exposures and failure. Whether a skin reaction occurs or not, the lapse of a certain latent period must precede any curative effect, whether superficial or deep. This peculiar slow action of the X-ray upon the living tissues is often a disadvantage when, because of urgent symptoms, a prompt change is desired.

In explanation of this peculiarly sluggish action of the X-rays many theories have been advanced. It is probable that alteration in cell metabolism, varying in degree with the radiosensitiveness of the type of cell, begins immediately after the absorption of the X-rays. This change progresses slowly toward degeneration and necrobiosis. It is only after a certain progress has been made that demonstrable tissue changes result. The more resistant cells recover before undergoing degeneration. When the disturbance in the local tissue metabolism gives rise to irritating and toxic decomposition products, the blood vessels become congested and a typical inflammatory reaction results. The liberation of cholin has been claimed by some investigators to be the cause of the inflammatory reaction. When egg yolk is irradiated, the lecithin is decomposed. The decomposition products, when injected into animals, produce in the skin necrosis and alopecia, in the testicles atrophy, in carcinoma and sarcoma softening. Cholin has a similar effect experimentally.

"Early" Reaction.—It has been often observed that, from a few hours up to forty-eight hours after an exposure, a peculiar redness of the skin may develop. This occurs most commonly after a heavy exposure. There may be itching, burning, and a slight erythema, resembling somewhat the true reaction. This early effect has been termed the "early" reaction or "preliminary" reaction. It differs from the true or late reaction in that there is no long latent period, that it is very transient, lasting only a few days, and that it never results in a true Roentgen dermatitis or the characteristic alopecia of the true reaction. It has, therefore, no clinical or prognostic significance, and need cause no alarm or cessation of treatments. It is believed to represent the reaction of certain more sensitive blood vessels to the degeneration products of irradiated cells.

"Cumulative Action."—The late appearance of the X-ray tissue changes, often the sequence of a long series of small exposures, has given rise to the term "cumulative action" of the X-ray. Although slow in beginning, the changes induced by irradiation are much slower in subsiding and ceasing. If such a cumulative action did not exist, and if the effect of each dose passed off rapidly, mild exposures continued over a considerable period of time could never accomplish anything. The effect thus accumulates in the cells until the maximum of tolerance or the saturation point is reached, and then the reaction occurs. A heavy exposure given a leukemic patient may produce a slow reduction of white

cells extending over several weeks. A full dose producing a vigorous reaction in a superficial epithelioma may result in a complete healing of the growth without further attention, although the process may extend over several months. This peculiar attribute of the ray may add to the convenience of X-ray therapy. For an efficient dose may be given over a period of a few days or a week, and the patient allowed to return home to await the reaction. Or, when patients live at a distance and frequent treatments cannot be given, one massive dose may be given every three weeks.

Theory of Personal Idiosyncrasy.—In order to explain the severe reaction occurring occasionally when the dosage did not seem excessive, the existence of an X-ray idiosyncrasy was claimed. As the therapeutic technique became better developed, evidences of idiosyncrasy became more infrequent. To-day its existence is denied by the best authorities. Such an idiosyncrasy would, of course, greatly impair the value of the methods of measuring dosage which are based upon the "erythema dose." X-ray effects which seem unusually severe for the supposed dosage administered can usually be traced to some inaccuracy in one or more of the factors determining dosage. The supposed existence of an idiosyncrasy has some significance from a medico-legal standpoint. While injury from Roentgen therapy is rare when given by competent operators, yet even the most experienced radiologist may occasionally produce unintentional effects, usually the result of an error in judgment. To forestall any such claim for personal liability in such accidents, some recognized system of technique should be followed, including a careful estimation of dosage. Complete records of the details of the treatment should be kept. Since the estimation of total dosage has numerous factors, such claims that the tube was placed too close to the skin, or that the time of exposure was excessive, can be shown to be invalid. When the condition under treatment is desperate, as, for example, inoperable carcinoma, intentional overdose may be sometimes justified. Injury to surrounding tissues due to failure to properly protect them from irradiation is always culpable. If the operator leaves the room during the exposure, the time of exposure should be controlled by an automatic time-switch, or an assistant or nurse should be left in charge. In either case the tube, meter, and patient should be observed at intervals from the protected booth or from an adjoining room.

X-ray Toxemia.—Of great clinical importance is the occasional occurrence of X-ray toxemia. The toxemia is directly traceable to the proteid disintegration incident to irradiation. While frequently so mild as to be unnoticed, it occasionally becomes so severe as to necessitate cessation of X-ray treatments, and the institution of general medical measures to control the same. When a large tumor mass to be disintegrated lies on the surface, much of the cellular débris may be discharged externally;

but, if the mass is deeply situated, the blood and kidneys must dispose of the degenerative products. The symptoms of the toxemia are, in the mild cases, simply a little malaise, headache, and pain in the limbs. In the more severe cases there are a rise of temperature, constipation, foul breath, and leukocytosis. The kidneys are affected chiefly and the urine, therefore, is the best indication of the condition. It may show all the changes, from a transient albuminuria to those of an acute nephritis. In the debilitated and aged such toxemia may be of grave import, while in the young and vigorous it is usually not a serious matter. The urine should always be watched in treating large areas, in giving deep treatments, or in treating such a general state as leukemia. Aside from the great clinical importance of these changes, the condition of the urine may be often taken as a guide in determining the amount of irradiation which the patient can tolerate. Fever and increase of nitrogenous constituents of the urine are the characteristic features of an X-ray toxemia.

Accompanying the symptoms of such toxemia there sometimes occurs (1 in 100 reactions—Holzknecht) a diffuse erythematous or papuloerythematous eruption. This eruption has been termed the "Roentgen exanthem." It may be local or general, and frequently starts from the area under treatment, and is usually transient in character. Such an exanthem, as well as the toxic symptoms, will occasionally result from very light irradiation. Severe intoxication may develop without the visible skin reaction.

The effects of the X-rays upon the body may be manifested in either the superficial or deep structures.

Effects on the Skin

In the skin three types of changes may occur:

1. Acute Roentgen dermatitis.
2. Chronic Roentgen dermatitis.
3. Late changes and sequelæ in irradiated areas.

Acute Dermatitis.—The acute dermatitis develops after a latent period of 2 to 28 days. Four stages have been outlined by Holtzknecht. In the *first degree reaction* there are temporary alopecia and some superficial desquamation without redness or visible signs of inflammation. Such a change may be accompanied by a resorption of pathological tissue, disappearance of psoriasis patches, etc.

In the *second degree reaction* there is hyperemia of the skin with erythema, itching, infiltration, feeling of heat and tension, sometimes pain. As it subsides it leaves behind a slight brownish pigmentation and desquamation, followed by *restitutio ad integrum.*

The *third degree reaction* is characterized by an intense bluish-red erythema with swelling, bleb formation, exudation, and excoriation of

the skin, with partial destruction of papillæ, sweat, and sebaceous glands. There may be apparent *restitutio ad integrum,* but usually the resulting area is covered by a thin, dry, irregularly pigmented skin which, after a variable time, may be the seat of the late changes and sequelæ. The process when active is very painful.

The *fourth degree reaction* or deep burn is preceded by the changes outlined above, and results in an ulcer which for its base may have the subcutaneous tissues, the muscle, or even the bone. The ulcer is exquisitely painful, and the resulting cicatrix, if indeed the ulcer closes over at all, is contracted, atrophic, deforms the surrounding area, and is frequently the seat of later secondary changes.

In mucous membranes a somewhat similar series of changes may occur with redness, swelling, bleb formation, and ulceration. The conjunctiva is especially sensitive, and often reacts to very small doses.

This series of changes is not necessarily connected with X-ray therapy. The most profound therapeutic effects may be elicited without causing any reaction. If, however, a reaction accompanies the irradiation, either intentionally or accidentally produced, it should not progress beyond a reaction of the second degree. The clinical history and pathology of the severer grades of reaction and their possible sequelæ furnish the classical conception of the action of the X-ray upon the skin.

The changes may be characterized in a general way as sluggish. Their course is one of weeks, months, or even years, rather than of days. There is a slow development, an acme, and a slower decline. The more severe the exposure the shorter the latent period, the more rapid and acute the acme, and the slower the decline. The X-ray ulcer is indolent, exudes a profuse serous or seropurulent discharge, and is painful beyond all bounds. The severe ulcers tend to cover over with thick sloughs, which adhere tightly and remain unchanged for months. If separated, another and deeper one may form. In the more favorable cases the ulcer is covered with an irregular grayish membrane, and around the edges there is beginning healing. The process of cicatrization is slow in the larger ulcers, but much more rapid in the small areas. The resulting fresh scar is thin, smooth, and often milk-white, and altogether so characteristic that it can readily be differentiated from scars of other origin. Later, contraction may occur and the scar is then not unlike that following ordinary burns.

Chronic Dermatitis.—The chronic Roentgen dermatitis is seen chiefly in X-ray operators or technical workers, and is the result of the summation of a great number of very small X-ray exposures extending over a period of years. It does not commence abruptly, as do the acute types, but very insidiously. The clinical picture is that of a slowly developing *hyperkeratosis* without any accompanying inflammatory reaction. It occurs chiefly on the hands, sometimes on the face, as a peculiar dryness and rigidity of the skin. The normal folds become accentuated and a

slight hyperemia may be noticed, followed later by a brownish pigmentation. The nails may show longitudinal streaks. There may be a sensation of heat, itching, or pricking. Finally, with atrophy of the sebaceous glands, the condition of hyperkeratosis begins. The skin becomes uniformly dry, loses its subcutaneous fat, and becomes tightly stretched over the underlying parts. The nails become brittle and deformed, and may be lost and replaced by a thick keratosis. Then localized hyperkeratoses may appear upon a tender infiltrated base. The keratoses reappear as soon as removed, often ulcerate, or form painful fissures. Slight trauma causes fresh ulceration, and so the process progresses either to malignant degeneration or to healing, especially if the keratoses are freely excised, with the formation of atrophic scars.

Late Changes.—The possible late changes in irradiated areas are of especial clinical importance. The pigmentation is not of special significance. The early pigmentation due to deposition of hemosiderin crystals disappears readily. The late pigmentation occurring in the scars may last for months or years, and is due to a migration of pigment from the degenerated epidermal cells into the cutis, where it increases.

Alopecia may be temporary, following a first or second degree reaction, or permanent, following the severer reaction. Temporary alopecia is an accompaniment of a full erythema dose. However, repeated mild reactions may lead to atrophy of the hair follicles and permanent loss of hair. Regeneration of hair following the mild reaction begins in 6 to 8 weeks. Usually the hair returns in its natural color and abundance. Occasionally, however, it may be coarse and of a different shade.

Atrophy of the skin is a possibility to be borne in mind when superficial treatments are extended over a long period, especially if repeated reactions are produced. The technique of deep therapy efficiently guards against such a sequel. Only after such severe superficial treatment as, for instance, would be necessary in lupus need it be feared.

This atrophy is almost always accompanied by telangiectases, dilatation of the preëxisting capillaries of the superficial capillary network. They develop only after a considerable lapse of time, usually long after the reaction has subsided.

Malignant changes in the atrophic skin and scars following either the acute or chronic Roentgen dermatitis have occurred in a certain percentage of the older severe cases. These changes have partaken of all the characteristics of carcinomata, and, in some cases, when not excised early, have resulted in metastases and death. The term "X-ray cancer" has been applied to the condition, from which the faulty inference is often drawn that the X-ray causes cancer. Roentgen carcinoma does not differ from any other skin cancer histologically, and does not represent a distinct clinical entity. Malignant change in areas of lowered vitality combined, perhaps, with chronic irritation is a common clinical observa-

tion. Irradiated areas in which these malignant changes develop are simply areas of lowered resistance. The X-ray produces the dermatitis in which the malignant changes develop, and, therefore, bears only an indirect etiological relation to the cancer. Any one of the commonly accepted theories for the causation of cancer may apply to the malignant degeneration of an X-ray burn. The possibility of "X-ray cancer" developing as a sequel to modern X-ray therapy is an extremely remote one, since the severe acute and the chronic Roentgen dermatitis should never occur. Some cases have developed, however, in connection with long-continued irradiation of lupus. When we consider the obdurate and dangerous nature of lupus, the necessity for the most heroic measures to cure it, and the not infrequent development of malignant disease in old lupus areas which have not been exposed to the X-ray, the possibility of Roentgen cancer is not a contraindication to vigorous and long-continued irradiation.

Histological Changes in the Skin.—The histological changes on the skin as a result of the absorption of Roentgen rays may be summed up as follows (Scholtz): The X-rays affect chiefly the cellular elements of the skin, which undergo a slow degeneration. The fibrous and elastic tissue, the muscles, and cartilage are only slightly or not at all affected, and suffer chiefly as a secondary result of the cell degeneration and the accompanying inflammatory reaction. The glandular structures of the skin and the blood vessels are attacked less vigorously than the dermal cells. When the degeneration which attacks nucleus as well as cell proper reaches a certain grade, an inflammatory reaction occurs with dilatation of vessels, infiltration of leukocytes, etc.

The changes in the smaller and larger vessels are of considerable importance. When the absorption of X-rays has reached a certain grade there are degeneration and proliferation of cells, especially of the intima, and, to a less extent, of the media, which may result in a complete obliteration of the lumen of the vessel. Formation of new vessels which have more or less imperfect walls may occur. This imperfect blood vessel formation is probably a factor in the causation of the sluggish and imperfect repair following X-ray injury.

Effect on Deep Structures

The Blood.—Of the deep organs the blood and lymphoid regions are most easily affected, furnishing the most perfect examples of true selective action. The influence of the ray upon the blood and lymphoid tissues is many times more rapid and more vigorous than upon the skin. Indeed, surprisingly small doses may cause profound changes in the blood and blood-forming organs. The changes are especially characterized by their rapid development, the latent period in some instances being as

short as two hours, and rarely longer than twenty-four hours. The changes may be complete in three or four days, and complete restoration to normal may occur within a week.

The changes in the blood result from direct exposure of the blood mass itself, as well as from exposure of the blood-forming organs, the character of the changes, however, varying in certain details.

The influence of the ray upon the blood has been established, both experimentally and clinically. The work of Heinicke (1904) upon mice and guinea-pigs forms the classical experimental basis, although his findings have been verified and amplified by many later observers. Studies upon irradiated blood in connection with leukemia have formed the chief clinical verification of the X-ray blood changes.

A few hours after the general irradiation of animals there is noticed rapid increase in the white elements of the blood, which differential count shows to be due entirely to the polymorphonuclear elements, a true leukocytosis. But the lymphocytes, both small and large, are greatly diminished. Therefore, with the leukocytosis there is a lymphopenia. This special action upon the lymphocytes is in accordance with the selective influence of the ray upon the younger and more embryonal types of cells. The leukocytosis is explained as a positive chemotactic effect of the cholin, the disintegration product of the destroyed leukocytes. After a few hours, if some of the blood-making organs are included in the irradiation, the blood picture again changes. There is now a leukopenia, both polymorphonuclear forms and lymphocytes undergoing reduction, although the latter suffer the greatest relative reduction. This leukopenia is the characteristic X-ray influence upon the blood. Its duration and degree will vary with the number and severity of the exposures. If the exposures are discontinued, rapid regeneration follows.

In six to seven days after the exposure the normal blood picture is usually restored. When, however, the exposures are confined simply to the blood stream and do not include the blood-forming organs, there is lymphopenia, but usually no leukopenia, and the normal blood picture may be restored in twenty-four hours. It follows that, in order to produce a marked reduction in both forms of white cells, the spleen, bone marrow, and lymphatic glands must be included in the irradiated areas.

In contrast to the radiosensitive white cells, the red cells are very resistant. Only after the most severe exposures are they affected, in which case there may be degenerated and nucleated forms found in the blood. In the ordinary therapeutic applications of the ray, either for the reduction of white cells or other effect, no change in the red cells or hemoglobin need be feared. In treating the blood and blood-forming organs, the dose should always be less than the erythema dose.

Blood-forming Organs.—A summary of the Roentgen influence upon the blood-forming organs may be found in the experimental work of War-

thin, who showed that the Roentgen rays have a selective action on lymphoid, myeloid, and epithelial cells, causing nuclear disintegration, fatty degeneration, and necrosis, which may be followed by secondary fibroblastic endothelial proliferation.

Spleen.—The spleen is the most sensitive of the blood-forming organs. In irradiated animals the spleen shrinks rapidly, and on post-mortem examination appears shriveled and of a dark brown color. Microscopically there is a great increase in the normally scant pigment. The Malpighian bodies are very small and the cell content of the pulp much decreased, the pulp appearing rarefied and porous. This disappearance of lymphocytes and disintegration of lymphocyte nuclei may progress until practically all of the lymphoid tissue is destroyed.

Lymph Glands.—The changes in lymph glands and intestinal lymph follicles are likewise characterized by shrinking and disappearance of the lymphoid elements. The thymus reacts in a similar manner.

Bone Marrow.—The changes in the bone marrow are expressed in the degeneration of its specific cells. The lymphocytes are first affected, then, in order, the non-granulated mononuclears, the eosinophiles, the mast cells, and, lastly, the myelocytes and polymorphonuclear neutrophiles.

Of extreme practical importance in the irradiation of the blood and blood-forming organs is the fact that there is always evidenced a strong tendency to regeneration, which usually appears immediately after the exposures, rapidly repairing the damage done by the irradiation. The reparation is complete, unless the changes have been pushed too far. This same tendency to return to the *status quo ante* is also manifest in treating abnormal conditions of these organs, which explains the great frequency of the recurrences of symptoms and the difficulty of producing permanent changes by irradiation.

The Liver.—The liver is extremely resistant, intense irradiation producing no evidence of any change in the cellular structure of the organ. However, in newborn and adolescent animals marked changes which increase in inverse ratio to the age of the animal have been produced.

The Kidneys.—The renal epithelium is very resistant to X-ray exposures. Very heavy doses (3 or 10 times the erythema dose) applied directly over the kidney produce, in animals, a degeneration of the renal epithelial cells, with later fibrous overgrowth following the inflammatory reaction, so that the picture of an interstitial nephritis is produced. With the usual therapeutic or diagnostic exposures in man, no *direct* action upon the kidney need be feared.

Kidney changes produced in a different way, however, accompany irradiation of any part of the body. It was early observed that long exposures (four to five hours) result in death in small animals (rats, guinea-pigs, etc.) in from three to ten days, with symptoms of paresis and coma.

Exposures of small animals for one-half hour produce, first, slight nuclear changes in the renal epithelium, followed later by cloudy swelling and albuminuria, the degree of which bears a direct proportion to the amount of lymphoid destruction produced. In the animals exposed continuously until death more marked renal changes have been observed, the renal cells being diminished in size and cloudy (Warthin). In man therapeutic irradiation in certain pathological states, as leukemia and carcinoma, may be followed by general toxic symptoms and the urinary changes of an acute nephritis. It is apparent that the toxemia and renal changes are the result of the excessive strain upon the kidney in further decomposing and excreting the products of protein destruction. The urine in these cases may show, in addition to the signs of acute nephritis, decrease in the uric acid output. It is, therefore, believed that the intoxication incident to irradiation is the result of a sudden overwhelming of the organism with disintegration products. Early the intoxication may be due to alterations in metabolism produced *directly* by the disintegration products in the blood, and the urine may show no change. Later, however, the integrity of the kidney may become impaired and the intoxication may become more severe. Such an irritation of the kidney is all the more probable when we recall the fact that the action of the X-ray upon the glandular organs varies directly with their protoplasmic and metabolic activity, and that the nuclear substance is first attacked, liberating a class of decomposition products which are of themselves toxic and difficult to metabolize and excrete.

The practical conclusions to be drawn are that X-ray disintegration of proteid, and especially lymphoid material, may injure the kidney. Therefore, when there is present an infectious or metabolic intoxication or a preëxisting kidney lesion, X-ray exposures must be cautiously given. In the absence of these conditions, however, no such complication need be feared in administering the ordinary therapeutic irradiation.

The fact that such alterations in metabolism as outlined above may occur, and the fact that the X-rays act so energetically upon the blood and blood-forming organs, brings up the question whether the ordinary therapeutic exposures may not injure the blood or blood-forming organs, as well as the kidneys. It must be remembered that the profound blood changes previously described were observed either in *small* animals exposed to excessive doses over the *entire* body, or in leukemic patients in whom there already existed a pathological blood condition, rendering them especially susceptible to X-ray influence. After a series of experiments made to determine whether repeated localized exposures may produce any such undesirable effects, Peters concludes that the repeated irradiations of localized pathological conditions in man are not followed by appreciable injury to blood-forming organs or kidneys, when these organs are protected from direct radiation. Allowance must be made for the

fact that the exposures employed in experimentation upon small animals, whose body weight is but a fraction of that of man, are, in proportion to body weight, many times larger than ever given therapeutically to man.

Sexual Organs.—Of especial interest and importance is the influence of the X-ray upon the sexual glands, testicles, and ovaries. Experiments upon the testicles of guinea-pigs and rabbits carried out by Albers-Schönberg (1903) showed that X-ray exposures to the testicles rendered the animals sterile, and caused characteristic microscopic changes in the testicles. These experiments first called attention to the action of the X-ray upon the deeper glandular organs, and opened the way for deep Roentgen therapy. It further suggested the analogous action of the X-ray upon the ovaries, and thus led to the employment of irradiation in certain gynecological conditions.

The changes occur essentially in the germinal epithelium of the testicles. In small animals the earliest changes were elicited by one-third of the erythema dose. Complete sterilization was produced by larger doses up to twice the erythema dose. The progress of the degeneration is recorded in the seminal fluid. At first there is some decrease in the number of spermatozoa (oligospermia), then many dead or dying spermatozoa appear (necrospermia). Finally the seminal fluid shows only a few or an entire absence of any reproductive elements (aspermia).

The histologic changes are found to involve chiefly the spermatogenic cells, producing, first, an inhibition of spermatogenesis, then a degeneration, which is not uniform and rarely complete. In the degenerated areas there are always seen intact cell groups. The connective tissue elements are unaffected. There may be connective tissue proliferation, however, following the destruction of the parenchyma. Regeneration, as a rule, follows quickly after the cessation of exposures, starting from the scattered uninjured areas, and, unless the exposures have been excessive, normal spermatogenesis is again established. The spermatozoa are very resistant and are affected only after sufficient radiation has been given to completely destroy the germinal epithelium.

This series of changes, as confirmed experimentally in animals by many observers, may occur in all its details in man. It was first observed clinically by Phillip (1904), who intentionally sterilized a tuberculous patient. Brown and Osgood (1905) found oligospermia or aspermia in 18 technical workers. Since then there have been numerous confirmatory reports from many radiologists, who, after one to five years of X-ray work, noted an absence of spermatozoa in the germinal fluid. This X-ray sterility was found to occur only in the earlier workers, in those who were engaged in X-ray work before the necessity for protective measures and the adequate means of carrying out the same were generally known. Since the development of the technique of protection from the ray such injuries to X-ray operators have become rare. Of extreme sig-

nificance is the fact that, in practically all of the cases of sterility reported (including the 18 original cases of Brown and Osgood) in which the subsequent history has been followed, the sterility has disappeared in from six months to two years after either giving up X-ray work entirely or after observing the usual measures for protection. The fact that the changes in the germinal epithelium are, as a rule, temporary, and are followed by active regeneration, and the fact that Simmonds exposed small animals to the secondary radiations such as are developed in the average Roentgen laboratory for one year without producing demonstrable changes in the testicles, is reassuring to those actively employed with the Crooke's tube. It is the consensus of opinion that the recognized protective precautions will guard the radiologist from such injury. This peculiar action of the X-ray upon the testicles is important from two clinical aspects. Can the usual therapeutic irradiations be carried out without injury to the testicles? Is it possible and practical to employ X-ray exposures to produce sterility? With proper technique injury to the testicles coincident to X-ray exposures of other parts of the body should never occur. The testicles should always be protected from the direct rays by a ray-proof covering, and from strong secondary rays as well. If direct exposure to the scrotum is absolutely essential, the possibility of such testicular changes should be explained to the patient. It is, however, not practical to produce sterility by X-ray exposures. While it is possible to destroy the entire spermatogenic epithelium by irradiation, the dose required would seriously injure the overlying skin. It has been shown that the cells nearest the source of the rays are chiefly affected, and that the deeper cells usually escape. Therefore, unless the dose be excessive and dangerous, there would be rapid regeneration following the exposures. Furthermore, the spermatozoa preëxisting in the tubules would not be affected by the usual therapeutic doses of the X-ray, which further precludes the practicability of producing permanent intentional sterility. The action of the X-ray upon the ovaries will be discussed in connection with the *special* X-ray treatment of uterine myomata.

Nervous System.—The nervous system is but slightly influenced by irradiation. It is true that small animals and especially the young of these animals may be killed in three or four days by excessive X-ray exposures. Warthin found that continuous exposures of five hours or more are fatal in ten days to mice, guinea-pigs, etc. The terminal symptoms may be convulsions, paralysis, and coma. Whether such symptoms are due to direct action upon the nervous system is doubtful. The progressive development of the symptoms suggests rather an intoxication from the products of protein destruction. No constant histological changes in the central nervous system following X-ray exposure have been established.

In man the nervous phenomena following X-ray exposures are extremely rare, only a few scattered reports of headache, sleeplessness, etc., have been recorded. The brain tissue and cord are apparently very resistant to irradiation. Furthermore, they are well protected by a heavy bony covering. No cerebral symptoms have been noticed even after the most prolonged series of treatments about the head. The nervous symptoms occasionally attributed to irradiation occur for the most part in neurotic individuals, and are undoubtedly of hysterical origin. That the X-ray may, however, effect pathological conditions in the nerve tissue is evidenced by the successful X-ray treatment of syringomyelia.

The Eyes.—The action of the ray upon the eye has been much discussed. Intense irradiation of the head of small mammals produces severe conjunctivitis and superficial keratitis. Very heavy doses, up to eighty times the erythema dose, produce iritis, degeneration of the retina, and optic atrophy.

A few reports of changes following irradiation of the human eye have been recorded. The changes have been found in the choroid and retina. In contrast to the few recorded cases of ocular changes following therapeutic X-ray exposures is the almost uniform experience of radiologists, that the region of the eye can be irradiated for months without injury. Belot, Kienbock, and others report large series of successful irradiations of lupus and carcinoma about the cheeks, eyelids, and orbits without producing any demonstrable impairment of vision. The results of experimentation upon small animals cannot be applied directly to man, for reasons that have been previously mentioned. The possibility of such injury, however, should always be guarded against by employing all practical methods of protection, and the irradiation of the region of eye and orbit should be directed with great caution. The danger of untoward effects following conservative irradiation is not tangible enough to preclude or interfere with such X-ray therapy about the eye as may be indicated. The human conjunctiva reacts very quickly to X-ray exposures, and the treatment may be often interrupted by a violent conjunctivitis.

Effect on Tissues of Young Children and Embryos

Since the X-rays in large doses cause interference with karyokinesis, atrophy, and degeneration of the cells of adult tissues, it follows that the tissues of young individuals and embryos will be similarly and more intensely influenced. A more intense effect is to be expected because of the selective action of the rays upon young and rapidly proliferating cells.

A variety of animal experiments bears witness to this action. In young animals the X-ray inhibits proliferation and stunts the development and growth. Exposure of newborn rabbits caused stunted general de-

velopment, as compared with unexposed controls. Exposure of one wing of a young chick caused imperfect development of feathers. Of especial interest is the inhibition or interference with osteogenesis. The fore legs of young animals were restrained in growth by irradiation, remaining much shorter than the hind legs. The development of internal organs is likewise interfered with by irradiation. X-ray exposures of the head of young animals not only retard the local development, but produce disturbances of growth in all parts of the body.

The effect of the X-rays upon fertility and embryonal development, as studied experimentally, is a profound one. Irradiation of small mammals before or immediately after pairing reduces the percentage of conceptions. In the early stage of pregnancy X-ray exposures may produce resorption of the ovum or abortion. In the later stages of pregnancy irradiation tends to prolong the period of gestation. The litter born under such conditions may be healthy, but smaller in number than usual, or the young may die immediately or a few days after birth. Again, the litter may be stillborn and macerated. Intense exposures seem to kill the embryos, while milder exposures impair the viability of the young. In some few instances certain congenital defects or variations were produced. By prenatal irradiation von Hippel produced cataracts in young rabbits. Here again the analogy between the experimental results upon small animals and the clinical effects in man must not be too closely drawn. Aside from the excessive dosage in proportion to body weight administered in the experiments, the fact that the rate of proliferation and growth of the young of small animals is much more rapid than in man accounts for the more profound influence of the X-rays upon the reproductive processes of these animals. Nevertheless, much caution must be observed when exposing very young children and pregnant women. It has been positively proven that sterility cannot be produced in women by *ordinary* therapeutic exposures. Likewise, many X-ray examinations undertaken to diagnose pregnancy from the radiograph have produced no demonstrable effect either upon the period of gestation or upon the child. Irradiation of small infants (under one year) for the reduction of an enlarged thymus has not resulted in any untoward after-effect, as far as the cases have been followed, and one child so treated is now over five years of age. The large series of children treated by Sabouraud, Belot, and Bordier for tinea and favus of the scalp have in no instance shown undesirable mental or physical effects. As a general rule, however, unless the condition is urgent, it is preferable to wait until the child is 8 to 10 years of age before administering X-ray therapy.

A committee from the German Roentgen Society, appointed to investigate the possible effects of X-ray exposures upon the physical development of children, makes the following report (April, 1910): "To the inquiries, 119 replies were received. X-ray examinations of young

children were generally believed to be harmless. Only five cases of interference with growth following X-ray therapy could be gathered. The committee concludes that the danger of injury to young children is very remote. Repeated X-ray examinations and the usual therapeutic application may be regarded as absolutely safe. Very heavy doses, which would cause other injuries, such as deep burns, etc., may inhibit development, but such heavy exposures are not justifiable, and such injuries should

Effect on Bacterial Life

A question much discussed in the early part of the Roentgen era, but now rather definitely settled, is the action of the X-ray upon lower forms of life. Many experimenters have tested the influence of irradiation upon bacterial cultures, with almost uniformly negative results. Some few reports note an inhibition of the growth of certain types of bacteria, but all are very resistant to irradiation and can be destroyed only by enormous doses. Since such large doses would produce irreparable damage to the human tissues, the bactericidal action of the X-rays from the clinical standpoint is practically negligible. The same holds true for the pathogenic fungi and protozoa. The curative action of the X-rays in certain infections may be attributed either to a stimulation of tissue cells, or to an impairment of the tissues as culture media.

X-RAY THERAPY OF SPECIAL CONDITIONS

The Roentgen therapy of special conditions cannot be adequately discussed in these few pages, for there is no other one remedy applicable to the treatment of such a wide variety of diseases. Especial stress has been put upon the principles of technique and upon the biological action of the X-ray on the human tissues, upon which the indications for its use may be based. While of great value in the treatment of many diseases, the X-ray is a specific in but a few. In a majority of properly selected conditions the X-ray will, however, bring about a cure unaided. In many others it must be assisted by certain local and general measures. Again, the X-ray may be simply an adjuvant to other forms of treatment. It is to be regarded as one form of therapy with certain limitations as well as indications. Its rational application will not infrequently yield results obtainable in no other way. When indicated, it should be used at once, and boldly. Most of the conditions referred for X-ray treatment are usually very chronic ones which have been previously subjected to every other known form of therapy. Hence, X-ray therapy must be judged with the same tolerance as other remedies. There will be a cer-

tain per cent. of failures, even in those conditions in which irradiation seems especially indicated. There is a large group of conditions for which we have no satisfactory treatment of any kind, and in which irradiation is indicated, not because it will cure the condition, but because it will do more good than anything else. In estimating the value of Roentgen therapy in these conditions, the above fact must be borne in mind. All things considered, the Roentgen ray is one of the most widely applicable and one of the most valuable curative agents in our therapeutic armamentarium. Success in its applications depends, aside from a mastery of the technique, upon a proper selection of cases, in which a correct diagnosis has been made and the pathology carefully considered.

Dermatology

In dermatology the X-ray has been accepted as an essential therapeutic agent, used as a routine measure by a few, but more commonly as an aid or as a last resort after the usual remedies have failed. The X-ray may be one of several methods of curing a certain lesion. Its painlessness, convenience, and cleanliness often commend it above salves, irritating applications, etc. Also, from the economic standpoint, irradiation is often preferable. The application of salves and various external medications often interferes with the earning capacity of the patient. This is especially true when the medication is odorous or demands bandaging, and when the lesions are on the exposed parts of the body. X-ray treatment will not prevent the patient from performing his usual duties.

The technique to be used in dermatological work is that of superficial irradiation. The tube used should be a low one, since soft rays are usually indicated. It should have a parallel spark gap equivalent of 1 to 3 inches, depending upon the nature and thickness of the lesion to be treated and the character of change desired. Such tubes will read from 2 to 4 on the Walter scale. The milliamperage employed will vary with the character of the apparatus at hand. Since stability of vacuum is desired, it is rarely practical to send more than 2½ milliamperes through a tube for any length of time without overheating. Where the tube is unseasoned 1 M.A. may be used. If the tube is well seasoned and perhaps water-cooled, currents of 2 to 5 M.A. may be used.

The time of exposure will vary with the method of dosage employed. If a chromoradiometer is used, 1/5 to 2/5 the erythema dose (1 H to 2 H) may be given at each treatment. If the milliamperemeter and equivalent spark gap is utilized to gage dosage, a working formula, based upon previous experience, must be established by the operator for the apparatus and conditions at hand. A good plan is to give the efficient dose in 3 sittings, administering 1/3 of the erythema dose at each exposure. These figures refer to unfiltered irradiation. When a filter

is used the time may be increased greatly, perhaps doubled. The target-skin distance should be comparatively small (5 or 6 inches) for maximum efficiency.

The dermatological conditions suited to X-ray therapy may be grouped according to effect desired. Only the more common conditions can be mentioned. As a rule, the X-ray is indicated only in *chronic* skin lesions. In acute and subacute conditions and in exacerbations of the chronic conditions X-ray exposures may serve only to irritate the process and are, therefore, either contraindicated or are to be used with the greatest caution.

Chronic Eczema.—Chronic eczema often responds most promptly to irradiation. In the acute stage the X-ray is not indicated, but when the skin changes incident to the continued inflammation have appeared and tend to remain stationary, the X-ray produces most brilliant results. Those cases which have resisted all forms of medication seem to be most energetically affected by the X-ray. No remedy relieves the itching as does the X-ray, for which purpose it may be cautiously applied, even in the subacute forms. Especially good results are obtained in the trade eczemas and eczemas on the hands and feet in general. In vulvar and anal types of eczema irradiation will often control the itching and give satisfactory results. Where the eczema is due to such underlying constitutional states as anemia, gastrointestinal disturbances, etc., or where some direct cause is demonstrable, such systemic states must be appropriately treated and all apparent sources of irritation removed, otherwise the irradiation may produce only temporary results. As to technique, it must be remembered that those forms in which the process is superficial and has caused no firm infiltration of the skin are susceptible to irradiation, since this chronically inflamed tissue is very radiosensitive. Therefore, in the very superficial dry or weeping forms, very cautious exposures to produce mild stimulation should be given. In the more infiltrated and thickened forms (eczema rhagadiforme, eczema tyloticum) heavier doses up to 3 H may be given. It is practically never necessary to excite an erythema. Small doses repeated every four or five days give the best results. As to recurrences, the results following irradiation are perhaps better than with other forms of medication, especially if a few mild prophylactic exposures be given after the lesion is entirely healed. While employing X-ray therapy, no other local measures should be used.

Psoriasis.—Psoriasis is one of the most grateful of the dermatoses to irradiate. As to whether irradiation is indicated in every case, or whether it is to be reserved for obstinate cases, there is much difference of opinion. Certain it is that a mild exposure, 1/5 to 2/5 of the erythema dose, will dissipate most of the lesions. Where the lesions are old and the base much infiltrated a longer course of treatment with a somewhat higher tube will be necessary. Lesions which have resisted ordinary

treatment for years will often yield to a few X-ray exposures. The mussy, odorous character of the external medication which necessitates a cessation of the patient's occupation, especially when the scalp or hands are involved, often makes the X-ray method preferable. This advantage is especially appreciated in treating generalized psoriasis when the patient's entire body may be bathed in the irradiation from a fairly high tube placed at some distance from the body. Since the cellular infiltration of psoriasis is extremely radiosensitive, the X-ray dosage in the average case need never be great enough to produce erythema or general metabolic changes. Protective measures, except possibly in the male genital region, are not essential. The fresher the lesions the more prompt the response to irradiation. Only in the older resistant lesions is the erythema dose to be approached, and then always in fractional doses. The treatment of psoriasis of the scalp with proper control of dosage can be undertaken without fear of alopecia.

Changes produced by irradiation occur in the typical case after but a few days' time. The intense red color gives way to a yellow-brown tint. The scales become less abundant and fall off readily without punctiform hemorrhages. In eight to fourteen days the infiltration is usually gone, leaving a slightly scaly brown spot which, however, rapidly assumes the tint of the healthy skin. Recurrences are not prevented by the X-ray method.

Lichen Planus.—Favorable results may be obtained by irradiation of lichen planus. The influence of the X-ray consists in a diminution of the hyperalgesia and the itching, which alone may improve the nervous and general condition of the patient, as well as in a slow improvement of the skin condition. The radiosensitiveness of the lesion varies somewhat with the type of efflorescence, the plane type yielding more promptly than the acuminate; the verrucose type is very resistant. The dosage required in the plane and acuminate types is always under the erythema dose. It is, therefore, necessary to avoid any visible reaction. Exposures may be given in fractional doses of 1 to 2 H, repeated every seven days. In the verrucose type it may be necessary to produce a first degree reaction in order to cause exfoliation of the horny plaques. It may be necessary to repeat the exposures after four to six weeks. Recurrences are not prevented.

Glandular Diseases of the Skin

The changes produced in the glandular elements of the skin by irradiation form the basis for the application of the X-ray to a group of diseases in which the glandular elements are the seat of the lesion.

The changes consist in an inhibition of the activity, or a partial atrophy, of the sudoriferous and sebaceous glands. In this connection

it is well to emphasize the fact that oft-repeated reactions or repeated series of treatments, each of which falls short of the erythema dose, may produce a slow atrophy of the glandular elements of the skin after the treatments have been discontinued. The result is a dry, shriveled condition of the skin, with possible telangectasis formation which, on the face or hands, is very objectionable and disfiguring. In other parts of the body such a sequel is not of much consequence, especially if the condition under treatment is severe enough to justify such an after-effect. Such a dry condition of the skin often results from repeated series of prophylactic treatments of the chest following amputation of the breast for carcinoma. X-ray exposures of the face and hands should not be unduly prolonged, and, if prompt results do not follow, some other method of treatment should be substituted.

Hyperidrosis.—Hyperidrosis, especially of hands and feet, usually responds promptly to X-ray treatment. The intertrigo which so frequently accompanies the hyperidrosis of the axilla and groin will be likewise healed by the irradiation. Since the effect desired is only an inhibition of the functional activity of the sweat glands, the irradiation should be mild. Fractional doses of 1/5 H may be given three times a week without producing a visible reaction. A leather filter is here indicated. Bromidrosis and dysidrosis may be treated along the same lines.

Acne.—The most brilliant results have been achieved in the treatment of acne by irradiation. The rationale of its use depends upon the fact that, by X-ray exposures, the functional activity of the sebaceous glands can be diminished. Whether the X-rays should be used as a routine in the treatment of acne is a matter upon which authorities are not agreed. Certain it is, however, that the X-ray should be resorted to in every obstinate case which resists the usual external medication. The cosmetic results surpass those following the older methods, especially where incising, curetting, etc., are resorted to. In the pustular type the end result is often surprising. While the primary action of the X-ray treatment is upon the sebaceous follicles, causing closing of pores and a disappearance of the oiliness, the accompanying secondary effect upon inflammatory infiltrate and scar tissue formation is not unimportant. This secondary effect serves to complete the cure in the pustular and indurated types of acne.

The technique implies considerable experience and much care. If the condition is not pustular and the lesions and surrounding skin not much infiltrated, very mild exposures are indicated. One-tenth of the erythema dose may be given three times a week. The target-skin distance should be twice the greatest diameter of the area under treatment. A filter may be profitably employed, although not essential if all the factors of dosage are well controlled. The treatment need never be pushed to an

erythema, or certainly never beyond a faint blush, in the average case. After the first series of exposures (the total quantity just falling short of the erythema dose) an interval of two to four weeks should elapse to avoid the full effect upon the glands. Then the series may be repeated, if necessary. In the severe pustular and indurated forms the treatment must be given more boldly, and a mild first degree reaction may be necessary in obstinate cases. Very mild exposures continued over a long period of time, never sufficient to produce a pronounced reaction, are dangerous because of the possibility of atrophy of the skin as a late sequel. A third series of treatments or a third reaction is rarely necessary or advisable in these cases.

Eyes and hair should be protected. The entire face may be best exposed by four positions. With the face turned profile, an exposure may be given over right and left cheeks. Then one over forehead and nose, and the fourth over chin and neck, the head being tilted backward. A medium tube (Walter, 5-6) should be employed.

To aid in cure and to guard against recurrences, the systemic factors in the etiology of acne should be corrected. It is especially important to secure and maintain efficient elimination.

Acne Rosacea.—Acne rosacea is more resistant and the treatment more difficult. Here, in addition to affecting the sebaceous follicles, it is desired to dissolve the inflammatory products and obliterate the newly formed blood vessels. X-ray treatment, by affecting the pustules and the glands, may improve the condition and stop its progress. Some diminution of the hypertrophied tissue may also be achieved by persistent X-ray treatment. There are on record a number of cases of large rhinophyma which have been greatly improved by X-ray therapy. In this type the treatment must be pushed to the production of a marked reaction, which, after four to six weeks, may be repeated. The Roentgen atrophy is here desired, since it may obliterate the vessels and result in a more acceptable condition than that which preceded it.

Skin Diseases Arising in Hair Follicles

A group of skin diseases arising from pathological conditions of the hair follicles are especially adapted to Roentgen therapy.

Sycosis Simplex.—Of these sycosis simplex is most common and yields most promptly. The brilliant results so often obtained by irradiation are seen most frequently in the inveterate cases which have been subjected to the usual external medication for months or even years.

The action of the X-ray in these cases is twofold. The activity of the hair follicles is diminished, which may lead to temporary alopecia. The X-ray at the same time attacks the fresh granulation tissue and pus cells,

causing their destruction, and eradicates the germs in the manner previously referred to.

The treatment in the severe cases should be pushed to the production of the temporary Roentgen alopecia with or without a slight erythema. However, milder cases may be successfully treated without causing such alopecia. It is generally conceded, however, that complete epilation offers the best prospect of permanent cure without danger of recurrence. The hair returns in four to eight weeks after cessation of the exposures. Some authorities recommend the vigorous use of antiseptics in connection with the X-ray treatment. A mild antiseptic ointment or wash is all that is necessary in the average case.

The dosage must be boldly given to the first degree reaction. The tube should be of medium hardness. A filter may be used by the very conservative. The target-skin distance should be twice the greatest diameter of the area under treatment. The erythema dose may be given in three to five fractional doses. Owing to inability to irradiate all the inequalities of the area under treatment uniformly, some few remaining loose hairs may have to be removed by forceps. Epilation often follows in ten days after exposure, the latent period being shorter in diseased hair follicles than in normal ones.

Acne Keloid.—Acne keloid, a pustular folliculitis which occurs at the hair-line upon the back of the neck, may be successfully treated along the same lines. The hypertrophic scarring which usually accompanies this condition may be wholly, or in part, absorbed.

Tinea and Favus.—In *mycotic diseases of the hair follicles,* where prompt and complete epilation is essential to a cure, the X-rays find a most important application. Unless radical epilation is accomplished, an ultimate cure with freedom from recurrence in *trichophyton tonsurans and favus* is a matter of great difficulty, requiring months or even years. Since the root of the hair is inaccessible to external antiseptics, the hair must be removed *in toto* and the antiseptics must be applied to the hair follicle. No other method of treatment will produce such a perfect epilation as the X-ray, for, by mechanical epilation, the diseased hairs are apt to break off.

In crowded centers, as London and Paris, where large numbers of children are affected with tinea or favus, the care of such children may become a social and economic problem, owing to the difficulty and length of time of the treatment necessary to a cure. Sabouraud in Paris has developed a system of X-ray therapy for tinea tonsurans and favus that has been accepted and adopted as the best method which we have. It is based upon epilating the affected areas by giving the "erythema dose," or rather the dose that will produce alopecia with a minimum of erythema as gauged by his pastilles. The secret of success in this method consists in developing the technique to the point where just the amount of irradia-

tion required for epilation may be accurately measured. If the dose is too small alopecia may be incomplete; if too large there may result either permanent alopecia from atrophy of hair follicles, or an X-ray burn. Furthermore, it is essential that the exposure over the entire scalp be uniform. Owing to the curvature of the scalp, uniform irradiation requires a special technique, as has been referred to before. With this end in view the scalp is divided into a number of parts and each division irradiated separately.

The hair should be first clipped short, preferably over the entire scalp, so that small incipient patches may be detected. When there are but a few patches they may be treated by isolating them with localizing tubes of proper size, or lead shields; but when there are more than five scattered patches, the rule is to depilate the scalp completely. The prognosis as to freedom from recurrence is always better when the entire scalp is treated. Saboureaud divides the scalp into seven regions, and exposes each separately, then covers it with a disk of lead foil so that the rays do not touch it again, and thus no overlapping of areas results.

Kienbock and Adamson have modified the technique by dividing the scalp into five instead of seven regions. Owing to the larger angle of incidence, which diminishes the intensity of the X-ray at the margins of areas, the successive areas are not covered by lead foil, but overlapping of edges is allowed. Although the areas of exposure encroach on each other, the rays fall at such an oblique angle on these overlapped edges that the dose is thus equalized over the entire area and no injury results.

The center of the successive areas may be located roughly as follows: A over median line two inches from frontal margin of hairy scalp; B over vertex of skull five inches back of A; C just above lower border of hairy scalp five inches from B; D and E just above and in front of right and left ears, respectively. The face, neck, ears, and shoulders should be suitably protected. A medium tube, reading about Walter, 4, should be used, backing up about two inches of parallel spark. The target-skin distance should be six to eight inches, and the pastille should be suspended in the central axis of the ray, three to four inches from the target. To avoid error it is important to have the pastille accurately centered under the target. The pastille should be carefully protected from sunlight, during exposure, by black paper, and examined in subdued light. The aperture of tube shield or diaphragm should be such that the rays will diverge to a circle of six inches in diameter at the scalp. The time of exposure will depend upon the milliamperage of the secondary current. With different operators it varies from ten to thirty minutes for each area. The treatment thus requires a number of hours (four hours with Saboureaud's technique) for each patient; however, with this technique only one treatment need be given.

In two to three weeks the alopecia begins, and in four weeks is usu-

ally complete. During the epilation the head is washed daily and anointed with carbolized vaselin, or painted with 10 per cent. tincture iodin, to disinfect the loose hairs and prevent contagion. Within two months a new growth of hair appears, and usually without a trace of the previous disease. The fungi seem to drop out with the hair, and a cure is usually accomplished without any further antiseptic treatment.

The treatment by the single full dose is a heroic one, and can be carried out only by an expert who has every factor of dosage controlled and has had considerable experience. The method is, therefore, unfortunately not adapted to an occasional case of a dermatologist not conversant with X-ray technique.

The treatment of large numbers of children with tinea and favus of the scalp by French and English operators has furnished an excellent opportunity to observe what effect the X-ray may have upon the development of the brain. Indeed, the question of possible injury following such heavy irradiation of the head has been raised. In a special discussion at a joint meeting of the dermatologic and electrotherapeutic sections of the British Medical Association (1909) the conclusion was unanimously reached that no such injury to the brain need be feared. This conclusion is of great significance to Roentgen therapy in general.

Tinea sycosis may be treated along the same lines as tinea tonsurans, except that it is not always necessary to epilate to produce a cure.

Kerion and Agminate Folliculitis.—The so-called *kerion* or deep suppurating hypertrophic folliculitis of the scalp, as well as the *agminate folliculitis* due to the trichophyton or similar fungi in any part of the body, are often amenable to proper irradiation.

Tuberculous Conditions

The value of the X-ray in *tuberculosis of the skin* is now well established. That the X-ray can cure tubercle formation in the skin is shown by the brilliant results in the treatment of the anatomical tubercle by irradiation. Numerous cases are recorded where a few vigorous exposures have caused prompt, complete, and permanent disappearance of the single "post-mortem" tubercle.

The action is probably threefold. The X-ray stimulates the resisting power of the tissues, as will be referred to in connection with the X-ray therapy of tuberculous adenitis. The X-ray also causes a reaction in the surrounding tissues, leading to a crowding of the vessels surrounding the lesion with leukocytes, which promotes absorption of inflammatory products and cellular débris and an infiltration of the tissues with small round cells, which tends to wall off the affected areas by connective tissue and favors repair. Finally irradiation causes actual destruction of the abnormal cells of the granuloma. Microscopic investigation by numerous ob-

servers has uniformly verified such changes in irradiated tubercles. The giant and epithelial cells are shrunken and degenerated, and finally disintegrated, while the surrounding infiltrate penetrates and cicatrizes the nodule.

Tuberculosis Verrucosa Cutis.—The X-ray has been successfully used in tuberculosis verrucosa cutis, where there are much papillary hypertrophy and hyperplasia of the epidermis, with perfect cosmetic results.

Lupus Vulgaris.—The application of the X-ray to lupus vulgaris is somewhat more difficult. In Europe, where the Finsen therapy is more extensively and intensively practiced, certain types of lupus vulgaris are treated by phototherapy from the start; others are referred to the Finsen institute to complete the cure after the disease has been brought to a certain stage by irradiation. In America the X-ray is generally relied upon alone, and the favorable results obtained by certain operators who have mastered the details of X-ray technique seem to warrant the enthusiasm which they evidence for this method of treatment. The apparent discrepancies in therapeutic results, as recorded by different writers, may be often traced to their lack of skill in administering the dosage, usually underdosing and abandoning the treatment too early. Finsen treatment has its advantages, and may be necessary to complete the cure in certain cases. Because of its greater penetrating power, the X-rays are more applicable to the deeper lesions and also to the more extensive lesions, where Finsen treatments would have to be of great duration. Finsen therapy cannot be applied to the cavities of the nose, mouth, etc., and is much more expensive than Roentgen therapy. Furthermore, Finsen therapy is not applicable to painful ulcerated surfaces. For these reasons Roentgen therapy is usually to be preferred. Both methods are, of course, painless, and give satisfactory cosmetic results.

X-ray therapy is especially indicated in the ulcerated and hypertrophic forms of lupus. The smooth, dry form with distinctly visible nodules is often resistant to irradiation; and on the Continent is the type that is usually referred at once to the Finsen institute. The hypertrophic lupus tissue can usually be broken down by vigorous irradiation, and the dry tumid forms are easily controlled. In the ulcerated forms the open area is usually promptly scarred over. Such a change greatly improves the appearance of the patient, thus giving him new hope, a factor not to be overlooked in treating the disfiguring types, where the mental condition is one of extreme depression. But when the lesion is scarred over the disease is not always cured, for in this area, especially under glass pressure, distinct nodules, which were perhaps previously invisible, can usually be seen. Now the treatment is centered over each nodule and the intervening tissue is protected.

The progress of reducing the hypertrophic masses to the level of the skin, and of causing the ulcerated areas to close over, is usually rapid

under irradiation, but from this stage on the treatment is often slow and difficult. Some cases can be healed only to this point by irradiation, and the remaining nodules in the upper layers of the skin require Finsen therapy or excision.

The treatment is necessarily a long one, and a cure in three months would be a very quick one. Some cases demand treatment for several years. Recurrences must be watched for and are not uncommon. Difficult of treatment are such cases as have been previously treated by curette and cautery, and especially so are the recurrences in the old scarred areas.

The prognosis as to cure and freedom from recurrence will depend greatly upon the relation of the local lesion to the systemic condition. Skin tuberculosis, which represents simply a local infection and in which the general health is good, will be influenced more favorably than those lesions which are accompanied by or are a part of tuberculous processes in other tissues of the body.

Tuberculosis of the Mucous Membranes.—Tuberculosis of the mucous membranes, especially of the hypertrophic type, often yields to mild irradiation if the location does not present technical difficulties which prevent proper administration.

Lupus Erythematosus.—Lupus erythematosus is very resistant to the X-ray. Absolute cures without recurrences are not easy to bring about. The usual discoid lesions of lupus erythematosus are notoriously resistant to all forms of therapy, and, after all others have failed, a resort to the X-ray may not be without avail. Often rapid improvement occurs, and even if the results are not absolute and permanent a trial of irradiation is warranted.

Heavy dosage and marked reactions are necessary to healing. Repeated reactions need not be feared because of the danger of producing Roentgen atrophy of the skin, for lupus erythematosus in its natural course is followed by atrophic scarring.

The best results are obtained in the fresh superficial forms of lupus erythematosus. If a mild inflammatory reaction is excited there is reabsorption of the effused infiltrating cells, the swelling diminishes, and the thin white atrophic scar of lupus erythematosus begins to appear. But the older, deeper forms, with thickening of the skin and abundant greasy scales, are less satisfactory to treat.

Scrofuloderma.—The X-ray is especially indicated in the treatment of scrofuloderma. Since the condition is usually a local expression or a sequel of an underlying tuberculous focus in lymph glands, bones, or other deep tissue, the underlying lesion should receive appropriate treatment, surgical or otherwise. The soft granulations are rapidly dissolved, and the ulcerated area scars over. When fistulæ are present, they may likewise be healed, if not too old and deep. If the underlying cause

is a broken-down lymph gland, it may be favorably influenced at the same time. For the fistulæ with very thick walls a preliminary curettage or excision may be necessary.

Diseases of the Skin Due to Fungi

Blastomycosis—In blastomycosis the X-ray has been found a valuable curative agent. In Chicago, where the disease was first discovered, irradiation combined with the administration of potassium iodid is the accepted treatment.

A pronounced X-ray reaction usually hastens the complete disappearance of the lesions, and in many cases the external application of antiseptics, and occasionally curetting of the thick papillary growths, will be necessary to a cure.

Mycosis Fungoides.—Mycosis fungoides has been favorably influenced by irradiation. According to recent reports, symptomatic cures are possible by X-ray therapy. The mycofungoid tissue is extremely radiosensitive. After an erythema dose with a medium tube the secretion diminishes and the itching subsides or disappears completely. The tumor masses shrink and finally disappear. But local irradiation does not prevent recurrences and metastases, and the disease is always fatal. The X-ray is the best measure, however, for the local lesions, and may prolong the life of the patient.

Benign Growths

Keloid.—In the treatment of keloid the X-ray is a valuable remedy, in spite of the fact that scar tissue is very resistant to irradiation. Because of this great resistance it follows that the dosage must be heavy.

Irradiation is applicable to all forms of scars, whether following burns or other trauma, or whether of spontaneous origin. Practically every case can be influenced, but all cases cannot be cured. In the favorable cases the elevated areas are converted into flat flexible white scars. In some cases, especially where the keloid is in the region of joints, or where, because of its tendency to contract, the scar embarrasses movement, the X-ray may be used to soften the scar, loosen it from the surrounding tissues, and thus make the whole area more flexible.

It is sometimes advisable to surgically remove the keloid previous to irradiation, especially if the scar is very thick. By such a procedure much time is saved, for many months may be required to dissolve the thicker keloids by irradiation. In the thinner and especially the more extensive types, such an operative procedure is unnecessary and inexpedient from the surgical standpoint.

The treatment of keloid by the X-ray is necessarily a long one, re-

quiring from several months to a year in the thick, extensive cases. A reaction is practically always desired, but it should be a mild one, especially if the lesions are on the face or the exposed parts. Repeated reactions may be elicited at intervals of four to six weeks. The tube should be somewhat higher (Walter—6) than that used for superficial therapy. The thin epidermal covering over the keloid is best protected by using the leather or aluminium filter.

Malignant Diseases of the Skin

The application of the X-ray to malignant disease dates back to 1899, when Stenbeck first irradiated epithelioma. Since then great numbers and types of malignant processes have been treated by X-ray exposures, and the results observed and recorded. Opinions have swayed from optimism to pessimism, and much unreliable literature has been created. To-day, 12 years after the introduction of the X-ray in the treatment of malignant disease, we are in a position to comprehend more clearly what the X-ray will do, and to make an unbiased estimate of its value in the war upon malignancy.

There is no doubt that the X-ray exerts an essential selective action upon cancer cells and destroys them. The degenerative process has been studied microscopically and comparisons made between exposed and unexposed areas of the same tumor mass. The protoplasm of the irradiated cancer cells becomes vacuolated, and does not take the usual stains, and the cell walls disappear. The carcinoma epithelium is penetrated by small round cells and leukocytes. Finally, the cancer cells disappear entirely, being replaced by a round-celled infiltration, which rapidly organizes. Thus the malignant mass atrophies and disappears, and is replaced by connective tissue. Around the normal edges an inflammatory reaction occurs, always secondary, however, to the cancer cell degeneration, and brings about repair.

Cancer cells of different types may be radiosensitive in varying degrees. Thus basal-celled growths of the skin are usually more promptly influenced than prickle-celled. But any cancer cell may be destroyed if it can absorb enough X-rays. The problem in X-ray therapy of malignant tissue then resolves itself into the administration of the efficient dose. If the lesion is superficial, massive irradiation is possible and easy. If the growth is deep, however, efficient irradiation is almost impossible, for reasons which have been previously stated.

It follows, therefore, that the very superficial growths should be readily destroyed, and clinical experience verifies this deduction. In superficial epithelioma the X-ray finds its most brilliant application. By epithelioma, as suited to X-ray therapy, is meant primary slow-growing cancer of the skin, which shows little or no tendency to metastases.

Whether the type be the flat, the papillary, the crater-form epithelioma, or the rodent ulcer, the results following irradiation are usually favorable. But it will not cure every case, nor is it indicated in every case.

Superficial Epitheliomata.—The X-ray is not the only method of curing superficial epithelioma, but the end results of X-ray therapy *in properly selected cases* will bear comparison with any other form of treatment. The X-ray method has much to commend it. It is painless and agreeable to the patient. The ordeal of an operation is obviated, which, in the aged, may be an important consideration. It is applicable to lesions which are not adapted to surgical interference, either because of their location, as, for instance, about the nose and eyes, where by excision too much tissue would necessarily be sacrificed, or where the lesion is so extensive as to make it impossible. The conservation of tissue incident to X-ray therapy is often surprising. The X-ray seems to spare all of the healthy tissue, destroying the diseased tissue around and even under it. An advantage not to be overlooked is the cosmetic result following removal by X-ray, which is usually better than, always as good as, that following the older methods of treatment.

The flat and the papillary forms are most susceptible to Roentgen therapy. The type in which the epidermis is not involved and covers the growth unbroken usually offers a favorable prognosis. Because of the intact epidermal covering, this type is not suited to treatment by the knife or caustics. By irradiation the underlying malignant proliferation can usually be destroyed and absorbed without producing more than a slight erythema of the skin, and without a scar. The crater-form types are usually more refractory. In the deeper ulcerated forms with indurated edges and fibrous base excision is usually the best procedure. The neighboring glands are usually involved early in this type of growth, and many of the recorded failures under X-ray therapy have been of this type. Some lesions, perhaps one in ten, may be refractory because of their histological makeup, or unsuited to the X-ray therapy because of the peculiar location of the growth, depth of tissue involved, or tendency to metastasis.

There is no conflict between X-ray therapy and the surgical treatment of superficial epithelioma. One should supplement the other. In some cases, because of a liability to metastasis or because of the existence of metastasis, radical excision with dissection of the involved lymph gland area should precede irradiation. Again, because of the size of the growth, excision or curettage may be done preliminary to giving X-ray exposures. Such a procedure may not only shorten the period of treatment, but also spare the patient the toxemia incident to the absorption and excretion of a large quantity of cellular débris. When in doubt, the lesion should be treated as a deep carcinoma (which see).

A large apparently inoperable malignant process in the skin may, by

irradiation, be reduced to a point where it becomes operable, and the knife may be resorted to in the removal of certain deeper involvement which the X-ray will not reach. Again, the X-ray may follow the surgical removal either to guard against recurrence and metastasis or to remove or check such recurrences and metastasis.

The prognosis under X-ray therapy in any case of superficial epithelioma is not favorable if there is involvement of the adjacent glands, or if it is in a location where early glandular metastases are known to occur. Such cases should be radically excised and then irradiated. The relation of metastases to X-ray therapy will be more fully discussed in connection with deep cancer. Since the metastases usually occur in the deeper tissues, i. e., the lymph glands, they can rarely be irradiated *efficiently*. Unfavorable are those cases occurring at the mucocutaneous junction involving the mucous membrane of the lower lip and cheek, and early excision followed by post-operative irradiation is the safest procedure. About the eyelids the results are usually good, even though the conjunctival mucous membrane be involved, for the orbit is not usually invaded. Those at the inner canthus are most liable to invade the orbit. If the orbit is involved a prompt and radical eventration should be done.

Epithelioma of lip and tongue and the mucous surfaces in general should be radically operated at once. Because of their tendency to early metastases in the deeper glands, they are to be classed with the deep carcinoma. A few favorable results from X-ray therapy in epithelioma of the lip, probably in the border-line cases (usually a papilloma just undergoing malignant change), have been recorded, but they do not justify delaying operation. The X-ray is of no avail in epithelioma of the tongue except in inoperable cases.

A cure is, of course, impossible unless metastases are prevented; or, if already present, checked and removed. Before instituting treatment in any case the field should be carefully surveyed. The favorable and usual sites for glandular metastases should be widely exposed as a prophylactic measure, using a higher tube and a filter. In comparing methods it must be borne in mind that the tendency to, and presence of, metastases make the prognosis bad for operative as well as X-ray therapy.

It is frequently observed that the malignancy of the new growth varies with its location. A prickle-celled epithelioma on the lip will readily involve the submaxillary glands and must be surgically treated, whereas a similar growth on the scalp will run a more benign course and will be amenable to X-ray therapy. The outlook is not so favorable in epithelioma developing on a chronic eczema or lupus base.

The administration of the X-ray in skin cancer must be bold. The overconservative technique so often employed by dermatologists accounts for many failures. If the lesion be ulcerated or uncovered by healthy epidermis, a fairly low tube (Walter—3 to 4) may be employed. The

target-skin distance should be about six inches. If the tube passes 2 milliamperes, a full erythema dose may be administered in five treatments of ten minutes each. If there is much uninvolved skin over the growth, or if the epidermis continues unbroken over the growth, a filter may be employed. The surrounding skin must be protected, but 1 centimeter or more of apparently healthy skin should always be exposed. Failure to observe this precaution will result in residual or recurrent nodules in the marginal skin, and greatly prolong the time and increase the difficulty of a cure. Such residual nodules in an elevated indurated margin often follow a faulty technique. The exposures may have been too mild or the penetration of the tube too great, and, after the center of the lesion is apparently healed, this slow-growing elevated edge will remain and is often refractory to irradiation.

When the reaction appears the treatments should be suspended. If necessary, a second or third reaction should be excited, but always awaiting the subsidence of the previous one. Likewise, when improvement of the lesion begins, treatments should be decreased or suspended. If they are continually pushed up to complete healing of the growth, a burn may result owing to the cumulative action. Many cases, especially the flat or papillary types, will progress to a complete cure after the administration of the full erythema dose, although the healing may not be complete for one to two months after cessation of treatments. Such an instance was recently observed, in which a large, partly flat and partly papillary epithelioma was given 6 H and the treatments suspended because of the vigorous reaction. The patient did not return for three months, during which time the effect of the X-ray continued and resulted in a complete cure.

After the cure is apparently complete the patient should return every two months for observation. Small recurrences usually respond promptly. They should be energetically treated, for, if there are *repeated* recurrences after irradiation, the lesion may finally become refractory to the X-ray.

Deep Carcinoma.—No operable deep carcinoma should be treated primarily by irradiation. By deep cancer is meant any malignant process which is not primary in the skin, or which involves subcutaneous, glandular, visceral, or osseous tissues. In the border-line cases of superficial growths which tend to go deep it may be difficult to determine whether the lesion will yield to irradiation. In every case in which there is the slightest uncertainty the knife should be resorted to first, unless such circumstances as extent and location of lesion should render operation inadvisable.

The X-ray, however, plays an important part in the treatment of deep malignancy. It may be used as (1) palliative measure in inoperable cases; (2) prophylactic post-operative measure.

In *inoperable cases* much comfort and a prolongation of life may

often be afforded by X-ray therapy. In these cases the irradiation may be valuable: (1) in relieving pain; (2) improving the local condition. These effects are especially marked when the lesion is located in a fairly superficial and accessible region. In certain deep locations, as, for instance, the viscera, and in certain regions where the blood and lymph supply are abundant, as, for instance, the neck, rapid growth and metastases are rarely influenced by irradiation.

Where there are foul and sloughing ulcerations the X-ray may cause them to clear up and heal over. In some instances the local lesion may close and partially disappear. At the same time the pain subsides and may entirely disappear. Thus the general condition of the patient, and especially the mental state, may be ameliorated. In inoperable cancer of the tongue, the local ulceration and swelling and pain may be improved by irradiation, and the patient may thus be enabled to take food. In spite of the local improvement and relief of pain from irradiation in these inoperable cases, there are always sooner or later the usual metastases into neighboring glands or distant organs, and ultimate death. The exitus is often made more bearable when brought about by a general and often painless asthenia than when occasioned by toxemia from a local sloughing mass with its attending pain, or by starvation, as in cancer of the tongue.

In the treatment of the inoperable cases, the exposures must be heavy and the technique well mastered. All the technical aids which will increase the intensity of the rays in the depths of the tissues may be utilized. The filter is indispensable, and the growths should be exposed from various directions, if possible. The various methods of desensitizing the overlying tissues or sensitizing the tumor mass itself may be tried. Evidences of toxemia must be carefully watched for. When large masses of tissue are to be broken down, it is often advisable to have a preliminary excision done with the least amount of shock, to prepare the field for irradiation. The amount of the dose is limited only by the amount that the overlying tissues will stand, and by the efficiency of the patient's excretory organs.

By far the most valuable indication for the X-ray in deep cancer is in the *prophylactic irradiation* following excision. The principle underlying such post-operative treatment is sound, but unfortunately not widely enough appreciated. When we consider the great percentage of recurrences that follow radical operation, even in cases that are considered surgically favorable, and then recall the selective influence of the X-ray upon cancer cells, it cannot but follow that post-operative irradiation gives the patient the best chance for ultimate recovery. Post-operative irradiation does not mean the X-ray treatment of recurrences, but the thorough exposure, up to saturation, of the field of operation, and the nearest lymph drainage areas shortly after the operation, and the repeti-

tion of such dosage two or three times during the following twelve months. The treatment is intended to inhibit the growth and destroy any malignant tissue, perhaps of microscopic dimensions, that has escaped the knife, and to "sterilize" and sclerose the neighboring glands and lymph channels. That the X-ray will affect such malignant remains is evidenced by the rapid disappearance of visible recurrent nodules under X-ray exposures. The absence of absolute proofs of the efficacy of such treatment against recurrences is not a valid argument against the routine post-operative irradiation of all patients. Proofs of the efficacy of such a line of treatment cannot be produced at this time, and perhaps not for some time to come, first, because this plan of treatment is comparatively recent, secondly, because recurrences may not manifest themselves until many years have elapsed, and, finally, because post-operative irradiation is not always carried out efficiently, since it must be given by a competent radiotherapeutist and must extend over a considerable period of time, implying an intelligent coöperation on the part of the patient, not always obtainable.

The application of the X-ray must be a routine one, since the surgeon can scarcely distinguish those cases in which ablation has been complete from those in which recurrences are probable. If administered unnecessarily to many patients in whom the ablation has been complete, the procedure is justified by the smaller percentage, or even occasional case, that may be spared from recurrence by such treatment. If the exposures are unnecessary, no harm has been done, and the exposure need not be a serious objection, since the success of the whole operation depends upon the prevention of recurrence. To wait for recurrence before applying the X-ray is to begin a battle that is half lost, for the prognosis under X-ray therapy is infinitely worse if demonstrable recurrence has already taken place. The recurrences are often deep and out of reach of anything approaching efficient irradiation, and are often much more intractable than the primary growth.

The post-operative prophylactic irradiation is not equally efficient in all points of the body. Because of its superficial location and the superficial location of its lymph drainage area, carcinoma of breast is best suited to this treatment. Likewise, after operations upon the skin, lips, and tongue, efficient prophylactic irradiation may be carried out. It is, of course, futile after resection of the pylorus, rectum, or uterus. In the latter instances exposures may be given through the vagina or rectum, but a sufficiently wide area can hardly be exposed to reach all of the lymph glands possibly affected.

If recurrence has occurred and is operable, it should be excised before beginning treatment. Superficial ulcers which remain after the wound is closed may often be successfully treated.

The prophylactic treatment should be begun about two weeks after

the operation. Deep exposures with a fairly high tube should be given through a filter, raying widely all the areas of possible metastases. The target-skin distance should be at least twelve inches. Giving 1 H at each exposure (the pastille must, of course, be under the filter), an efficient dose may be given in ten treatments. A maximum dose should always be given. Anything less is useless. Such a series of treatments should be repeated two or three times during the ensuing year. Prophylactic post-operative irradiation does not guarantee freedom from recurrence, but, in conjunction with an early and radical operation, it is the best safeguard of which we know.

Sarcoma.—The treatment of sarcoma by the X-rays must follow in a general way the plan outlined for deep carcinoma. But sarcomata exhibit in their reaction to X-ray therapy some striking differences from carcinoma. While certain types of sarcoma represent the acme of malignancy from the surgical standpoint and rapidly recur after operation, these same types may show a surprising sensitiveness to irradiation. It is found that soft, cellular, rapidly growing tumors react more promptly than the slower growing connective tumors. Round and spindle-celled sarcomata are more easily influenced than osteo- and chondrosarcomata. The rapidity with which certain types of sarcoma will decrease under irradiation is surprising. Especially favorable to treat are those originating in the skin and in the lymph-glands. There is such a variation in the malignancy of sarcoma that it is impossible to predict what success will attend the X-ray treatment. A sarcoma of the deep lymphatic glands of the neck may be sometimes influenced to a symptomatic cure by irradiation, whereas a superficial growth in a location apparently more favorable for X-ray therapy may show only unretarded growth under the treatment. Therefore the treatment of sarcomata cannot be considered complete without resort to the X-ray at some stage in its course. It need hardly be emphasized that for operable cases early radical excision is always indicated. Especially valuable is X-ray therapy in mediastinal sarcomata. Pressure symptoms are often relieved and temporary symptomatic cures have been obtained.

In inoperable cases X-ray exposures may afford some relief from pain and may bring about local improvement as in carcinoma. Post-operative prophylactic irradiation is positively indicated. A close coöperation between surgeon and radiotherapeutist is essential to the greatest measure of success. In the borderline cases where the operability of the growth is doubtful it is sometimes advisable to test the sensitiveness of the growth by a few X-ray exposures before operating. If the influence of the X-ray is prompt and marked it may be continued.

The technique of the therapy is analogous to that for deep carcinoma. Owing to rapidity of growth of these tumors exposures must usually be given daily. They must be massive almost up to the point of producing a

burn. Only an expert radiotherapeutist will be capable and courageous enough to administer the heroic doses that are essentially required.

Lymphatic and Blood Diseases

The high radiosensitiveness of the *lymph glands, lymphoid tissue, blood,* and *blood-forming organs* furnishes the basis for X-ray therapy in a variety of affections.

Tuberculous Adenitis.—In tuberculous adenitis its value is generally recognized. The favorable influence of irradiation in this condition may be due to the well-known selective nature of the X-ray upon lymphoid tissue, and especially when that tissue is in a state of chronic inflammation attended by rapid and abnormal proliferation. According to Pirie, the X-ray destroys the rapidly developing giant cells. Other observers consider the effect of the X-ray to be a stimulation of the metabolism of the affected glands, producing hyperemia and increased phagocytosis.

There are some grounds for believing that irradiation may produce serological changes analogous to autogenous vaccination. The existence of such a process is evidenced by the occasional observation that unexposed tuberculous glands will decrease in size during irradiation of neighboring or distant similarly affected glands. Upon this basis X-ray therapy has been applied to obstinate *furunculosis* and *venereal buboes* with some favorable results, and any infectious enlargement of lymph glands may, if resistant to other therapeutic measures, be subjected to trial irradiation.

X-ray therapy in tuberculous adenitis is especially indicated when the enlargement is fresh. Glands which have not yet reached operable size, or which are just enlarging to operable size, usually respond to irradiation. Glands which have reached the operable stage but have not yet begun to suppurate often subside under X-ray treatment. Frequently, however, the larger glands will break down, and it is usually safer and more expeditious to excise the lymph chain or, at least, the larger glands before beginning treatment. Older glands which are about to undergo caseation, or in which caseation has commenced, are less favorable to treat. X-ray therapy in these cases often hastens the softening. Glands which have suppurated and are practically circumscribed abscesses should be excised and then irradiated.

The X-ray method possesses certain inherent advantages. It is of course painless and avoids the shock and dangers of a tedious operation which the general condition of the patient may preclude. It penetrates the affected area throughout and searches out glands that may escape the operator or that may be infected without being visibly enlarged. Thus in a measure it guards against recurrence. By its action the glands are reduced to hard fibrous nodes, the size depending upon the amount of previous inflammation, connected by fibrous bands representing the re-

mains of the lymphatic channels. Upon section these hard bodies are found to be composed entirely of fibrous tissue, all glandular structure having disappeared. Complete disappearance of the glands does not follow irradiation. When the glands have reached the stage of small shotlike bodies, and when all signs of local inflammation have disappeared, the treatment may be discontinued. The sclerosis of blood vessels and lymph channels in the irradiated area is the best safeguard against spread of the infection and recurrences. The cosmetic effect following X-ray therapy should be perfect, since the tanning incident to the administration of the maximum dose will disappear in a few months. During X-ray therapy it is not necessary for the patient to remain in a hospital. He can be following out the proper hygienic measures which are so important in this disease.

There should be coöperation between surgery and X-ray therapy in these cases. The X-ray may be a valuable adjunct to any type of operation. The difficulty of the technique of the radical operation, the tendency to recurrence, the poor general condition of the affected patients, which sometimes precludes a tedious radical operation, may be the indications for X-ray therapy. If a complete operation is done post-operative irradiation may lessen the chances of recurrence. If only an incomplete operation is possible the X-ray may often be relied upon to complete the cure. In the old chronic cases with "matting" of tissues which precludes a thorough operation the X-ray may heal the sinuses and promote sclerosis. It is often advisable, in *very feeble* children for instance, to excise only the larger glands of the affected area, leaving the rest for X-ray therapy.

The technique of the X-ray exposures is that of deep irradiation. A filter is absolutely essential. The exposed area should extend wide of the disease. In the neck the entire region from the base of the skull to, and including, the apex of the lung should be treated. A hard tube at a distance of twelve inches passing two milliampères of current may be used. Ten treatments of ten minutes each given three per week will deliver an efficient dose. After the reaction subsides a second or third series may be given. No other local medication should be permitted while under X-ray treatment, as it may produce changes in the skin and confuse the estimation of dosage.

Leukemia.—The report of the first case of leukemia treated by X-ray exposures was published in 1902 by Pusey. What seemed destined to be a specific for this hitherto incurable disease proved, however, to be only a palliative measure. Although uniformly prompt improvement resulted from X-ray exposures sooner or later recurrences followed which would yield only temporarily to further treatment; and ultimately the cases became refractory. No authentic case has been cured by X-ray therapy up to the present time. From an analysis of the mode of action of the X-ray in this disease it is apparent that by irradiation only the symptoms and

not the ultimate cause are affected, and that the X-ray does not, at least by the present method of administration, offer any prospect of eradicating the disease. Notwithstanding this fact, however, the X-ray method promises a more prompt, certain, and uniform symptomatic improvement than any other known form of treatment, and likewise offers the best prospect of prolongation of life.

The X-ray is indicated in the chronic forms of both splenomedullary and lymphatic leukemia, the results being much more favorable and easier to attain in the former than in the latter. In the acute and subacute forms of leukemia the X-ray is strongly contraindicated, since it will not avail anything, and may serve to hasten the exitus. The prognosis under treatment is better in the young than in the aged and debilitated.

The action of the X-ray in leukemia is manifested upon the blood, spleen, liver, lymphatic glands, and upon the general metabolism. The action upon the white blood cells is both quantitative and qualitative. In the splenomedullary types the number of white cells sinks with a rapidity that is often surprising. Practically every case can be influenced, although not with the same promptness nor to the same degree. In one case reported by Grawitz the white cells were reduced from 1,250,000 to 8,000 under a six weeks' course of X-ray therapy. In a favorable case it may be possible to reduce the white cell count to a figure approaching the normal. When the normal is approached the exposures should be stopped. Under no circumstances should a leukopenia be produced, although by the usual technique the irradiation can be rarely given efficiently enough and without injury to the skin to produce a leukopenia. Analogous but less striking reduction in the number of white cells may be obtained in the lymphatic type.

More important as an evidence of improvement, as a guide to the treatment, and as a prognostic factor are the qualitative changes. The X-ray acts most energetically upon the more rapidly growing and more embryonal types of blood cells. The unripe myelocytes which normally do not leave the bone marrow are rapidly destroyed, and may be reduced from 50 per cent. or 60 per cent. to 30 per cent. or 20 per cent. during the first series of treatments. By vigorously pushing the exposures the percentage of myelocytes may be reduced to 2 per cent. or 3 per cent. or they may even disappear entirely. Such an entire disappearance is not always possible to attain and is of course only temporary. The polymorphonuclear neutrophiles and the lymphocytes are likewise absolutely decreased but relatively increased. In the lymphatic types the qualitative changes are not so easily brought about, and in order to reduce the lymphocytes to their normal qualitative proportions it may be necessary to produce an absolute leukopenia, which is always objectionable and not easily brought about.

Not infrequently a preliminary increase of the white elements is noted

early in the course of the treatment, usually following heavy exposures. The anemia which accompanies the leukemia may be improved under X-ray treatment, and the erythrocytes and the hemoglobin content may increase during the irradiation, such an increase being of good prognostic import. The nucleated reds may likewise decrease in number or disappear entirely.

The spleen usually decreases rapidly in size, and when the enlargement is slight may return to normal size. In the usual case, however, only a moderate decrease in the size of the spleen can be brought about by irradiation. In rare cases it cannot be reduced at all. In every case it tends to enlarge again after treatment is suspended. The lymphatic glands likewise decrease in size under X-ray treatment and the liver may shrink, although always more slowly than spleen or lymph glands. When the mediastinal lymph structures are involved this action of the X-ray upon the lymph glands may serve to relieve distressing and dangerous pressure symptoms.

Associated with these changes in the white blood cells and lymphoid tissue there are greatly increased metabolic activities as evidenced by certain changes in the urine. The uric acid output is greatly increased during the period of active cellular destruction. Its amount during the twenty-four hours may reach one to three grams. The purin bases and the phosphates are likewise much in excess of the normal. The condition of the urine may be an important guide as to the progress of the case and in determining the required dosage. Excessive amounts of nitrogenous débris may cause toxemic symptoms, and in the early stages of the treatment such signs must be cautiously watched for.

The amelioration of the general condition of the patient, which usually follows so promptly under X-ray treatment, justifies the utilization of this method aside from any other considerations. The patients feel stronger and the mental depression and apathy often disappear. The varied symptoms associated with the anemia improve or disappear. The bone pains are relieved and the patients gain weight and may be able and anxious to follow some light occupation. The decrease in spleen and liver makes the breathing easier and relieves the embarrassed stomach and kidneys. In the lymphatic types such marked changes do not always follow irradiation, especially if the patient be past fifty, nevertheless some improvement can usually be noted.

The technique employed in the X-ray treatment is an all-important consideration. Upon a rational conception of the nature of the disease and the mode of action of the X-ray must depend the measure of success attained by X-ray therapy. The action of the X-ray is expended, by its selective tendency, upon the pathological lymphoid proliferation. If this proliferation be of bacterial etiology the amount of radiation reaching the deep tissues cannot possibly destroy the causal germs. The rationale of

the X-ray therapy can best be explained upon the assumption that the leukemias are a kind of new growth, a sarcomatosus. X-ray exposures of spleen and lymphatic glands destroy the young, sensitive cells, chiefly mononuclear leukocytes and myelocytes in these structures, and the size of the organs is thereby decreased. Heinecke showed by microscopical examination extensive nuclear destruction occurring in a leukemic tumor as early as seven hours after irradiation. General toxic disturbances such as fever, headache, vomiting, etc., may result from this cellular disintegration. With this extensive destruction of cells in spleen and glands part of the dense infiltration emigrates from the spleen and lymph glands into the general circulation and may produce a temporary increase in the white count early in the treatment. This "poussée leucocytaire" (Aubertin and Beaujard) is soon followed by a great decrease in the number of white cells in the circulating blood brought about in several ways. Aside from the actual destruction of white cells in the spleen and lymph structures, which process also occurs, but in a much less degree, in the circulating blood itself, there is apparently developed in the blood a substance (myelotoxin) which inhibits, and may completely stop (temporarily), the further proliferation of abnormal cells in the bone marrow. With this decrease in the production of cells there is a decrease in the amount of poisonous products developed and a corresponding improvement in the general condition of the patient. This feeling of well-being often occurs before there is any appreciable change in the blood count. Most important in this complex process is the development of a leucolytic ferment in connection with the leukocytic destruction, which further dissolves the white cells, chiefly the mononuclear leukocytes and myelocytes, even in areas which have not been irradiated. Linser and Heller showed that blood serum from an irradiated animal, when injected into an unexposed animal, produced leukopenia, and that leukocytes irradiated *in vitro* gave a like effect. Capps and Smith showed that serum from an irradiated leukemic patient produced leukolysis in another unexposed leukemic patient.

The early American and all of the foreign operators exposed simply the spleen and lymph glands with little attention to the bone marrow, since it was evident that the bone marrow was simultaneously, although indirectly, affected by the serological changes in the blood, and that exposures of the bone marrow alone would not produce the desired decrease in size of the spleen and lymph glands. Pancoast in this country has come to somewhat different conclusions. Assuming that disturbance in the bone marrow is the ultimate cause of the disease, and that the changes in the spleen and lymph glands simply represent metastatic processes, he concentrates his efforts primarily upon the bone marrow. It has been experimentally proven upon animals that the X-ray can produce atrophy of the bone marrow. Pancoast, in contrast to certain German observers,

produced a reduction in spleen, although more slowly, by exposures of the bone marrow alone. He therefore advises exposing the bone marrow primarily and most vigorously and attending to the spleen and other structures later. In this manner he hopes to avoid much of the toxemia and the temporary rises in the white count which so often accompany heavy primary exposures of the spleen. If we regard the bone marrow as the primary focus of the disease and the lymphatic enlargements as secondary foci Pancoast's plan of treatment commends itself. A further argument for the soundness of this plan is the fact that, in Pancoast's series of cases, he found that the patient may regain an almost normal state of health and vigor with the leukocyte count remaining high and the secondary enlargements nearly of the same size as in the beginning.

The technique of the X-ray exposures in leukemia is that of deep irradiation. A filter must always be used. If we adopt the Pancoast method the body may be divided into definite areas including as much of the skeleton as possible, but avoiding the spleen and the head. These areas may be successively exposed, one each day. The danger of injuring the skin is thus much reduced. If the treatments are concentrated upon the spleen primarily as recommended by most German operators the exposures should be made from various directions, front, side, and back. The center of the organ may thus absorb an amount of irradiation which no one area of the skin could withstand. In the lymphatic type the enlarged glands as well as the spleen must be irradiated. The method of treating the spleen and lymph glands energetically from the start brings the most marked and quickest improvement. Whether under this method relapses are more frequent and the prognosis more unfavorable than under the bone-marrow treatment of Pancoast cannot be determined until more extensive comparative statistics are available.

Certain it is that under any plan of treatment great caution must be exercised. Systematic blood examinations are essential. When the leukocyte count approaches the normal treatment must be suspended, although Pancoast contends that the differential count is the more important and that if possible a normal differential count must be striven for, as the disease cannot be considered temporarily checked until such normal relations are brought about. The aim of the X-ray treatment is not solely the reduction of the white cells to the normal, but the general condition of the patient should also be a guide. The total quantity of X-rays to be administered must depend upon the general condition of the patient, especially as regards metabolism, and upon the tolerance of the skin. When the greatest possible improvement seems to have been reached treatment should be suspended, to be resumed again as soon as a rise of leukocyte count or an increase in the percentage of myelocytes gives warning of an impending relapse. Long periods of rest from the X-ray therapy are not

advisable. The patient must remain under constant observation and the whole number of treatments may reach a high figure.

The prognosis under any form of X-ray therapy must be regarded as unfavorable, and occasionally under the treatment there will be fatal relapses or apparent conversion from the chronic to the acute type of the disease with prompt exitus. Each relapse is usually more refractory than the preceding.

In pseudoleukemia with symmetrical lymph gland enlargements (*Hodgkin's disease*) the X-ray offers more hope than in leukemia, and the prognosis as to cure is not always unfavorable. Some cases are favorably influenced. The lymphatic enlargements may decrease, or even disappear, although the latter is not the rule. Usually some hard nodes remain. The anemia often improves, and if there is a leucocytosis the white count may return to normal. There are certain types of the disease which are absolutely resistant to the X-ray, and the heaviest exposures produce no apparent change on the local enlargements or the general condition. The spleen is not so markedly affected as the lymph glands. Regarding the lymphatic enlargement as a modified type of sarcoma the difficulty or impossibility of eradicating the disease and the great tendency to local recurrence or distant metastases make the treatment under any method a hard task. The enlargements are often in invisible and in inaccessible locations, which makes efficient irradiation impossible.

The writer recalls two such cases in which the cervical enlargement promptly disappeared, only to be followed by metastases. In one case apparently normal health was enjoyed for a year and a half, when intrathoracic pressure symptoms developed and a radiograph revealed a large mediastinal tumor. In the other case a deep epigastric tumor appeared six months after the cervical glands had subsided.

In the cases with mediastinal masses the pressure symptoms may be relieved or dissipated; and in treating cervical enlargements the mediastinum should always receive attention as a prophylactic measure.

The technique is similar to that of sarcoma. If the case is a favorable one for X-ray therapy the enlargements subside with surprising rapidity.

The group of allied, but imperfectly classified, conditions of anemia with or without splenic or lymphatic enlargements may be briefly discussed together.

Lymphosarcoma.—The so-called lymphosarcoma or malignant lymphoma may be treated along the lines indicated under sarcoma. At least local and temporary improvement is usually attainable.

Banti's Disease.—In Banti's disease the recorded results from X-ray therapy are favorable, although only few cases have been treated. Regarding the spleen as the primary focus of disease the treatment should be directed chiefly to this organ. In the published reports a decrease in

the size of the spleen and some general improvement are noted. In one advanced case treated by the writer the spleen was reduced to about one half its original size, although not to normal dimensions, and there was a great improvement in the general condition. The enlarged liver, however, can rarely be markedly influenced by irradiation. The effect upon the spleen in this condition is more slowly brought about and with greater difficulty than in leukemia, because the enlarged spleen in Banti's disease is largely fibrous in its nature and therefore of low radiosensitiveness. Likewise in *splenic anemia* the spleen cannot be profoundly affected by the X-ray exposures, and the change produced, if any, is very slight. Here, too, the radiosensitive splenic pulp is already atrophied and replaced by radioresistant cirrhotic or amyloid tissue. The blood condition in splenic anemia is not improved by irradiation, and the results therefore of X-ray therapy are not encouraging.

Polycythemia.—In *polycythemia* very little change in the blood condition has followed irradiation and the spleen is usually not reduced. Pancoast recommends exposures over the bone marrow in this condition rather than over the spleen.

Splenic and Lymphatic Enlargement.—In any splenic enlargement, especially of an obscure or unclassified type, a trial series of X-ray exposures may be given. When the hyperplasia is lymphoid in character a beneficial effect of varying degree may be expected. If the enlargement is due to degenerative and sclerosing processes the outlook is less promising.

Likewise the treatment of obscure lymphatic enlargements can hardly be considered complete without a resort to the X-ray.

Enlargements of the Glands

Mikulicz's Disease.—In Mikulicz's disease a special indication for the X-ray exists. Most favorable results have been obtained by irradiation in the five reported cases with complete symptomatic cure in three cases.

Goiter.—The X-ray has been extensively used in treating *enlargements of the thyroid gland* with only a moderate degree of success. The X-ray plays a part in the treatment of goiter only in so far as it affords a possible means of favorably influencing the gland in cases in which operation is contraindicated, inexpedient, or refused. It is generally conceded that the X-ray will not cause an entire disappearance of the thyroid enlargement, and that the best that can be expected, even in the cases especially suited to X-ray therapy, are a moderate decrease in the size of the gland and an improvement in the symptoms. The rationale of the treatment is based upon the fact that the X-ray inhibits the activity and causes atrophy of glandular structures. It follows, therefore, that the parenchymatous types with simple hypertrophy of the secreting tissue are more favorably

influenced than the fibrous, colloid, and cystic types. Where pressure symptoms are marked the reduction in the size of the gland is rarely sufficient to entirely relieve them.

In *exophthalmic goiter* a considerable improvement may be brought about by X-ray exposures. The improvement is chiefly in the toxic symptoms, rather than in the thyroid tumor itself, although the gland may be often reduced a third or more. By inhibiting the functional activity of the gland and causing a certain degree of atrophy many of the distressing symptoms of hyperthyroidism may be relieved. The tachycardia, exophthalmos, dyspnea, and all the varied nervous symptoms may improve. X-ray treatment is especially indicated where the severity of the toxic symptoms precludes operation. The fibrosis of the gland capsule and adjacent tissues which follows irradiation may increase the difficulty of a subsequent operation.

Results from irradiation of the thyroid are difficult to elicit and require a considerable time. Therefore, if the X-ray is resorted to, the trial should extend over several months at least before passing judgment.

The technique is that of deep therapy. A filter should be used and the exposures should be made from three different directions in order to safeguard the skin. Although we no longer look to the X-ray to cure goiter it is of great importance to have a remedy which, without pain and without the great danger so often attending operative treatment, will, in a measure, at least, control the toxic symptoms of this condition and reduce the size of the gland. Pfahler's statistics of 51 recorded cases of exophthalmic goiter treated by X-ray showed a marked improvement in 75 per cent. Schwartz's reports upon forty cases treated by irradiation at Holzknecht's clinic are favorable as to general improvement of nervous symptoms, but the goiter was reduced in only eight cases and the exophthalmos in only fifteen.

Prostatic Enlargement.—Attempts have been made to treat enlargements of the prostate upon the same basis that irradiation has been applied to enlargements of the thyroid. Owing to the inaccessibility of the gland and the fact that the enlargements are so often fibrous no uniform success has attended the efforts. In contrast to a number of favorable reports are perhaps a greater number of failures. When the enlargement is chiefly glandular some decrease in the size of the gland may be achieved. In the favorable cases reported a prompt improvement in the associated urinary symptoms has been noted. This method of treatment is still more or less experimental and should be resorted to only when surgical measures cannot be employed, as for instance in the very aged and feeble. The treatment is given through the rectum, directing the rays toward the gland through a speculum.

Enlargement of the Thymus.—In *enlargement of the thymus gland* the X-ray seems primarily and specifically indicated. The treatment will

be more fully outlined in consideration of treatment of status lymphaticus, and is mentioned here only to emphasize its value. The writer has had most favorable results from X-ray therapy in five cases of enlarged thymus in young children. The gland, whether of lymphoid or epithelial origin, seems to be very sensitive to irradiation, as verified by experimental X-ray exposures of the thymus of young rabbits. The changes produced in the gland by experimental exposures have varied from nuclear destruction of the small thymus cells to complete atrophy and fibrosis of the gland.

Diseases of the Respiratory System

Unresolved Pneumonia.—Based upon the well-known action of the X-ray upon rapidly proliferating embryonal cells some careful experiments were made by Edsall upon unresolved pneumonia. It was found that the leucocytic exudate in the lungs could be markedly influenced. The action of the X-ray upon the pulmonary infiltrate seems analogous to its action upon leukemic infiltrates. The cells of less resistance suffered degeneration and dissolution with a coincident improvement of physical signs and symptoms. As is uniformly observed in many other conditions, the rapid destruction of the cellular infiltrate was followed by marked metabolic changes. In the presence of a preëxisting toxemia the added disintegration products of the irradiated infiltrate may produce undesirable or dangerous toxic symptoms. It is therefore recommended that such exposures be employed only in afebrile cases. In the acute stage of pneumonia the X-ray is strongly contraindicated because of the resultant toxemia. This line of treatment is not recommended as a routine measure in unresolved pneumonia, but in selected cases a careful trial may be indicated.

Internal Tuberculosis

X-ray exposures have been used in the treatment of *internal tuberculosis,* but the results have, on the whole, been disappointing. The active influence of irradiation upon tubercles as evidenced in the X-ray treatment of the fresh tubercles of the skin cannot be elicited in the deeper regions. Whatever favorable effects may have followed X-ray therapy in deep tuberculosis must be attributed to a stimulation of the tissues to react against the infection. Perhaps the best results have followed the irradiation of *tuberculous peritonitis.* That this condition may be favorably influenced by proper X-ray exposures seems fairly certain, although the method has not been widely employed. It need hardly be mentioned that X-ray therapy should not displace or interfere with the proper surgical treatment. But as a post-operative measure, or in cases where operation is contraindicated, inexpedient, or refused, the X-ray may offer some aid.

Bircher, in 1907, studied 28 cases of tuberculous peritonitis, 16 of which were treated by operation followed by irradiation, while 12 were treated by irradiation alone, with unusually good results in both series. He concludes that the X-ray is an extraordinarily useful aid in the treatment of tuberculous peritonitis.

Nervous Conditions

Neuralgia and Neuritis.—The X-ray exerts a unique *influence upon sensory nerve endings.* It was very early observed that following radiographic examinations of painful conditions there was an amelioration or a complete relief from the pain. This analgesic effect was first attributed to the high-tension electrical field surrounding the tube, but it is now fairly certain that the X-rays exert a distinct action upon the sensory nerve endings, for relief often occurs from exposures too mild to produce any changes in the surrounding tissues. The indication for, and the value of, irradiation in many of the previously mentioned conditions depend in certain measure upon this analgesic action. This is especially true of the use of the X-ray in advanced malignant disease. Upon this basis the X-ray has been employed in the treatment of *neuralgia* and *neuritis.* In the so-called neuralgias, in which no cause is apparent, irradiation has been followed by favorable results. In such conditions, however, the pain can usually be influenced more surely by high-frequency currents or other methods of treatment.

Pruritis.—Analogous to the analgesic effect of the X-ray the *antipruritic effect* is often the prime consideration in applying the X-ray to various skin diseases. The relief from itching is often more prompt than the relief from pain, and may follow a single mild exposure. The X-ray has therefore been found of value in the treatment of *pruritis ani* and *pruritis vulvæ.* Here again the X-ray should be used conservatively only after other remedies have failed. The X-ray, however, will not cure every case of pruritis, and recurrences may follow an apparent cure. Especially favorable are those cases in which the skin is thickened and eczematous. The treatment should be undertaken cautiously and unless the technical factors of dosage are well under control a filter should be used. A medium tube is indicated. In treating the male perineum the testicles should be carefully protected. It is rarely necessary to produce an erythema.

Syringomyelia.—Perhaps the only disease of the central nervous system in which Roentgen therapy has found a place is syringomyelia. Favorable results have been recorded by nine observers, chiefly French, from the X-ray treatment of fifteen cases. The irradiation is believed to affect the gliomatous proliferation and thus relieve the pressure. Improvement of varying degree in both motor and sensory symptoms has been reported,

but no complete cures. This plan of treatment is of too recent origin to permit of an adequate estimate of its ultimate value, but in the absence of any satisfactory treatment for this condition the X-ray should be given further trials.

Deep exposures should be given over the cervical spine through a filter.

Influence Upon the Ovaries

Changes in the ovaries analogous to those produced in the testicle may be brought about by X-ray exposures. Because of the deep position of the ovaries these changes are much more difficult to bring about than those following exposure of the testicles; yet the ovaries are so susceptible to irradiation that it appears entirely practical to therapeutically influence certain clinical conditions through irradiation of the ovaries.

It was first shown by Halberstadter, in 1905, that atrophy of the ovaries in the rabbit could be produced by heavy X-ray exposures. His findings have been verified by numerous experimenters. In small animals marked changes in ovaries could be produced without causing even alopecia on the overlying skin. There were noticed a disappearance of Graafian follicles, decrease in size and number of primordial follicles. These changes were followed by regeneration and restoration of normal functions if the exposures were mild. After heavy exposures the gland became permanently atrophied and converted into a nonfunctionating fibrous mass.

The technical difficulties incident to the production of these changes in the ovaries increased with the size of the animals experimented upon. Thus in dogs much heavier exposures were required than in guinea pigs and mice. In the human female, owing to the absorption of rays by the overlying tissues and the danger of injuring the skin, the problem of efficiently irradiating the ovaries becomes more difficult. Yet numerous reports are accumulating in the literature of definite microscopic changes in the human ovaries following X-ray exposures. Most interesting is that of Fraenkel, who irradiated one ovary (the other being protected) in a woman who later came to operation. Both ovaries were removed, the protected one showing Graafian follicles and primordial follicles in all stages of maturation, while the ovary receiving the X-ray exposures consisted of fibrous tissue without follicles.

A great amount of clinical evidence as to the action of the X-ray upon the ovaries is to be found in the medical literature of the last few years. The chief therapeutic application has been directed to reducing and controlling *uterine myomata* by causing atrophic changes in the ovaries.

Albers-Shönberg gives the following terse summary of the action of the X-ray upon uterine fibroids, which is herewith quoted in part without comment:

(1) The ovaries suffer, from X-ray exposures, an atrophy especially of Graafian follicles, as a result of which an artificial menopause follows. This action is especially easily elicited in women near the menopause, with greater difficulty in younger women.

(2) The artificial menopause is accompanied by shrinking of myomata and a decrease of the associated hemorrhages.

(3) Intramural fibroids are best adapted to this treatment, subserous less so. In submucous forms this treatment is contraindicated.

(4) Anemic women with myocarditis, or so-called "myoma hearts," should not be irradiated. Fatal hemorrhage has followed X-ray exposures in such cases.

(5) Certain refractory cases will not yield to this treatment.

(6) Amelioration of the metrorrhagia and menorrhagia may follow, even when an artificial menopause cannot be produced.

(7) The tumors decrease in size, but rarely disappear.

(8) The especial domain of X-ray therapy is climacteric hemorrhages and pain.

Fraenkel, in a recent publication, attempts to systematize gynecological X-ray therapy by formulating certain theories to explain the results of irradiation of the ovaries. He advocates the use of the X-ray in menorrhagia, dysmenorrhea, female nervous manifestations of sexual origin, etc.

The production of sterility in healthy women not near the menopause by X-ray exposures has not been proven practical up to the present time. While it may be possible to ultimately produce complete atrophy of the ovaries in a young healthy woman the length of time and great amount of irradiation necessary to secure such an effect render the procedure uncertain.

The technique employed is that of deep therapy. The skin must always be protected by a filter. The treatment always extends over a considerable period of time and the number of exposures by the fractional method may be very large. The exposures are always given over the abdomen, target-skin distance 12 to 15 inches, penetration 6-8 on the Walter scale. Treatments should be given in series of five or six treatments each. Single exposures should equal about twenty milliampère-minutes. An interval of two to three weeks should elapse between each series. The superficial dose for each series, as measured by the chromoradiometer placed under the filter, should not exceed 4 H. A water-cooled tube, which will not drop in vacuum during exposures, is essential. The use of a compression cylinder, which will desensitize the skin by producing anemia, and will reduce the distance between skin and ovaries, is recommended.

To bring about more prompt and more certain changes in the ovaries a technique is being evolved by radiotherapeutists by which several times the erythema dose may be administered at one treatment without injury to the overlying skin.

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CHAPTER XII

PSYCHOTHERAPY

LOUIS CASAMAJOR

Psychotherapy, healing through the medium of the mind, is the oldest of established therapeutic procedures. Ever since primitive man began to search for the causes of his pains and other symptoms, and through them a cure, psychotherapy has been a part of most, if not all, therapeusis. At the earliest dawn of civilization the idea of external influences causing disease was predominant, and such influences were usually the wrath of the gods, or possession by demons. Prayers, sacrifices, and religious rites, then the first of therapeutic measures, were purely psychotherapeutic. The miracles of the numerous saints, gods, demigods, prophets, leaders, and other holy men that play so prominent a part in the folk lore and the literature of every race early established psychotherapeutic practices in the popular mind, and it was thus that the close connection between psychotherapy and the Church was founded. This relationship exists to-day to no small extent, as is proven by the fact that most of the "new" religious cults which are continuously springing up around us rely for their power of attracting and holding devotees mainly on the ability of this or that idea or "new thought" to cure disease—usually the functional disturbance of the nervous system.

This primitive, larval psychotherapy is without exception suggestion therapy, and it was not until comparatively recent times that the world knew any other form of psychotherapy but suggestion. Suggestive measures are used by all races, and their origin, like that of other superstitions, is, for the most part, lost in the dim obscurity of the beginning of races. The prophylactic and therapeutic use of charms and tokens is as old as man himself; nor have the advances of science and twentieth century culture succeeded entirely in replacing them. The greasy amulets and scapulars are so frequently seen by physicians, especially those doing dispensary work, that they rarely stop to reflect on their origin as charms against disease. The negro who treasures his rabbit's foot, and the farmer who carries a horse chestnut in his pocket to ward off and cure rheumatism, know and care as little about the origin of their idea as does

the fond mother who ties the amber beads around her child's neck to prevent the dreaded croup. Since time immemorial, the "hair of the dog that bit you" has been "good for hydrophobia." Even in this enlightened age magic stones and rings for the cure of disease are bought by the credulous. The boy, that prototype of primitive man, is firm in his belief in charms, for who, who has been a boy, does not hold in his memory some of those mystic means of removing warts!

Suggestion, then, has been the principal psychotherapeutic agent since the birth of therapy, and until lately has been the only one. Hence, it is fitting that we deal with it first, and leave the more modern reëducation for the later section. Psychotherapy as a broad subject may be divided, then, into three main headings, with subdivisions, as follows:

A. Suggestion Therapy—
   1. Simple suggestion in the Conscious State.
   2. Hypnotism.
B. Reëducation—
   1. The method of DuBois.
   2. Psychoanalysis of Freud.
C. Secondary Agents—
   1. Occupation.
   2. Exercises.

A. SUGGESTION THERAPY

1. Simple Suggestion in the Conscious State

Suggestion may be defined as the absolute acceptance of an idea as true without previously applying to it any critical reasoning or logic. It may be divided into two forms: autosuggestion, when the suggestion comes from the individual himself, and heterosuggestion, when the suggestion comes from others. Likewise, we may consider suggestion as direct or indirect. Suggestion is said to be direct when the idea is given directly, and of itself, to the patient without any intermediary agent. When one tells an hysterical patient that his arm is anesthetic, and it immediately becomes so, the suggestion has been direct. Indirect suggestion is that in which the idea is given to the patient in a roundabout way, or by means of a definite agent. The therapeutic workings of bread pills, placebos, etc., are instances of indirect suggestion therapy.

Suggestion causes as well as cures symptoms, and every one is suggestible to some degree. "The suggestible element," says Sidis, "is a component of our natures. It never leaves us, is ever with us." The suggestibility of normal waking life is usually not great, but in some

diseases, notably hysteria, it dominates the individual. In normal persons extremes of suggestibility do not exist in the waking state, and are seen only during hypnosis.

Naturally suggestibility is subject to great variations, not only between different individuals, but at different times in the same individual. Children are normally very suggestible, much more so than adults, and middle-aged people respond to suggestion better than those who are old. It is the common observation that women are more suggestible than men. Suggestion is a form of belief, or possibly the relationship may be reversed and the same rules obtain in both cases. The less an individual is accustomed to reason and to apply critical judgment the more susceptible he is to suggestion.

The variations in the same individual depend on his state of health and the capacity of his attention and his reasoning power. The increased suggestibility during illness has been a common observation from early times. Rabelais very accurately portrayed this fluctuation of suggestibility in the ordinary man when he wrote his well known couplet:

> "The devil was sick, the devil a monk would be;
> The devil was well, the devil a monk was he."

Autosuggestion practically does not exist in the normal individual, but it plays an important part in the causation of many hysterical symptoms and, notably, hypochondriacal manifestations. Suggestibility as a cause of the symptoms of hysterics, neurasthenics, and other neurotic individuals is a matter of daily observation to the physician. The bad effects wrought in some patients through ideas culled from the conversation of others, from the reading of medical books, or, worse, the so-called medical advertisements in the newspapers, are too axiomatic to call even for comment. Instances of severe illness and often of death itself, arising from simple suggestion, usually indirect, are so common that they are accepted without question by the world at large.

Suggestion since earliest times has been and still is such a considerable part of the armamentarium of every practicing physician, that it is often very difficult to draw the line between those cures occasioned by suggestion and those due to other agents. Not even surgery is free from suggestive influences. The beneficial effects which certain operations, notably those correcting uterine displacements and floating kidneys, occasionally have upon the functional nervous disorders may often be ascribed as much to indirect suggestion as to the physiological effects of the operation. Likewise, an understanding of the possibilities of suggestion as a therapeutic agent has, in recent years, changed to a large measure the attitude of the physician toward drugs and drug therapy. It is this realization of the power of suggestion, so forcibly brought to our minds by the

cures of various sects, "therapies" and "pathies," in themselves purely suggestive, which is responsible to a large degree for the therapeutic pessimism and nihilism which of late the younger physicians have been so frequently accused of.

Confidence of the patient in the physician has through all time been recognized as an essential for the proper treatment of the case, and this confidence is nothing more than the patient's susceptibility to the physician's suggestion. The indirect suggestion that goes with every drug prescribed to a conscious patient has more or less effect on the result. How much, it is often impossible to say. The vogue that this or that drug or method of treatment has had, and is still having, in neurasthenia and other psychoneuroses, testifies often more to the value of psychotherapy than to the power of the particular fad. The indirect suggestion which is such an important asset to cure resorts and healing springs is brought forcibly home when one reflects how inefficient these same treatments and mineral waters so frequently show themselves in the patient's home. It is hardly the province of the author to discuss or attempt to outline the psychotherapeutic value of drugs, hydrotherapy, electrotherapy, mechanotherapy, massage, etc., as a means of indirect suggestion, but one must always bear in mind that they all have in them an element of suggestion which is not inconsiderable in the production of results.

It is practically impossible for one to attempt to outline methods of giving suggestion to patients. Every physician who practices must necessarily utilize suggestion therapy more or less in his everyday life, and the method he employs is that with which he has obtained the best results, and in all probability differs markedly from that of his neighbor. The physician's personality and the personality of the patient naturally determine the method in which suggestion is given; for, while in one case the direct suggestion that this or that pain will disappear is frequently efficacious, in a second case such simple suggestion methods are of no avail, and arouse in the patient an antagonistic attitude.

2. Hypnotism

Historical Review.—Hypnotism as a scientific study is a development of modern times, but the phenomenon in itself was known to ancient races. Many of the sayings of oracles which so often influenced the course of ancient history were the productions of individuals in the hypnotic state. Thus, for instance, the Gnostic sect in Egypt in the second century, A. D., according to Brugsch-Pascha, obtained oracular utterances from persons in whom they had induced hypnotism by closing the eyes and stroking them. Æsculapius is said to have quieted excited patients and induced sleep in them by rubbing.

Paracelsus and his followers first began to speculate on the nature of hypnosis and applied to it the name "magnetism." They conceived of a magnetic fluid arising from magnets which one could project at will to anybody and thus influence his movements and state of mind. Gassner, a German priest, born in 1727, began the study of "magnetism" and its relation to disease, although up to this time the ideas of Paracelsus and his followers, especially Fludd, had been violently combated by the Church. In his work, principally with hysterics, he learned that catalepsy, anesthesias, paralyses, twitchings, blindness, deafness, and other symptoms could be caused to appear by his method as well as to subside.

Of all of the early investigators of the psychic phenomenon we now call hypnotism there is none more prominent than Mesmer. Franz Anton Mesmer was born in Germany in 1734, and died in 1815. At heart he was a mystic and filled with the fantastic ideas of the ancient alchemists and cabalists. In 1775 he visited Gassner in Regensburg, and observed his work and results, and thus began his own interest along these lines. The magic power of the magnet at first was to him the basis of the phenomena he observed, and he invariably used a small magnet as a means of inducing hypnosis. Later he found that the magnet was not absolutely essential, for he obtained the same results by stroking the patient's body with his hands from head to foot, and even by making passes with his hands near the patient, without so much as touching him. Reasoning by analogy, he conceived of an "animal magnetism" in contradistinction to "mineral magnetism," the active force of Paracelsus. This animal magnetism, according to Mesmer, was a fluid of inconceivable fineness which could be projected into others and influence them for good or for evil. The extent of the impression which Mesmer left upon human thought can be no better shown than by the persistence in the minds of many, even in this day of scientific accuracy, of the idea of "animal magnetism" of malicious intent. From this time on Mesmer's ideas dominated this branch of psychic study, and the name "Mesmerism" was given to the phenomenon we now call hypnotism. Petétin in 1787 describes a cataleptic state occurring from mesmerism.

Abbé de Faria (1814) brought new light into this dim realm of thought when he denied the existence of an animal magnetism, and stated that the phenomenon was brought about not by any external force, but by the mental processes of the patient himself (imagination). He discovered that mesmerism could be produced not only by rubbing the patients and by making passes over them with the hands, but also by having the patients look fixedly at his open hand while he repeated the word "sleep" with emphasis. This was the earliest use of suggestion in the induction of hypnosis. In 1821 Dupotet introduced mesmerism into the Paris hospitals.

Lafontaine brought hypnotism to England in 1841, and there it at-

tracted the attention of the surgeon Braid. He held firmly to the old idea of a magnetic force as the cause of the phenomenon, but he utilized ocular fatigue in having the patients look at an object held above the head in inducing "magnetic sleep." He was the first to recognize that one can bring magnetic sleep upon himself (autohypnosis). Braid used his magnetic sleep with good results in many diseases, and succeeded in performing operations painlessly while his patients were in this condition. When Braid discarded the magnetic theory he, in searching for a name for the phenomenon, called it Hypnotism.

In America Grimes began the study of mesmerism about one year later than Braid, but the work was not scientifically pursued by him at first. In fact, in its early days in this country, it was the stock-in-trade of traveling quacks who termed themselves "Professors of Electrobiology."

From this time on we must turn to France for the further development of hypnotism. In 1866 Liebault established a clinic for hypnotic therapy in Nancy, and, ten years later, Charcot and his pupils took up the scientific study of Hypnosis, especially in relation to the therapy of major hysteria in the Salpêtrière in Paris. By this movement Hypnotism was lifted from the realms of mysticism to the plane of a scientific study. The master mind of Charcot analyzed the phenomena, divided and classified them, and applied hypnotism systematically and with a definite purpose. It is to Charcot that we owe for the most part the knowledge of hypnotism which we possess to-day. The Salpêtrière school divided hypnotic states into lethargic and somnambulistic. These classifications are of only historic interest, and to describe them here would do little but confuse the reader.

After Charcot many scientists interested themselves in hypnotism, and the subject developed very rapidly. Space allows us to mention but a few of the more prominent names with which hypnotism is associated:

Babinski, Binet, Gilles de la Tourette, and Prosper Depin in France; Heidenhain, Burges, Binswanger, Krafft-Ebing, Obersteiner, Bernheim, Forel, Moll, and Löwenfeld in Germany; Jendrassik in Hungary; Bechterew in Russia; Lombroso and Morselli in Italy; Vincent, Kingsburg, and Bromwell in England; and Beard, Hammond, Beach, Mills, and Sidis in America.

Susceptibility to Hypnotism.—It is probable that every normal individual is susceptible to some degree of hypnosis, but authors are by no means agreed on this point. The individual reaction not only of the patient, but also of the physician, is necessarily very great, and this may account for the varying results obtained. The percentage of susceptible individuals which different authors have observed is given at anywhere from 30 per cent. (Bottey) to 100 per cent. (Vogt).

As a general rule, young people are brought to the higher degrees of hypnosis more easily than those of middle and advanced age. Possibly

women are more easily influenced than men, but in such a comparison between the sexes only those of the same educational attainments and temperament can be considered together. Sensitive, high-strung people are usually more susceptible than robust, muscular ones. Invariably uncultured, unthinking persons lend themselves more readily to hypnosis than do the educated, and the reason for this lies in the lack of critical reflection in the former. The serious-minded, as a rule, make good hypnotic subjects, while a facetious, jocular manner with a tendency to laugh forms a barrier practically insurmountable. Heavy drinkers frequently are very susceptible to hypnosis, and possibly this may be accounted for by the deterioration in critical judgment which often accompanies chronic alcoholism. Severe neurasthenics, to whom this method of treatment is so frequently applied, behave in the same way as do healthy normal individuals. The personality of the hypnotizer is a very important element in the susceptibility of the patient. It does not consist of any magic electric force of a personal magnetism, but rather of the impression he is able to make on the patient of his ability to bring on the hypnosis and to aid the patient. This fact alone can account in great measure for the higher percentage of susceptibility reported by some observers, as well as for the much better results obtained in cases by specialists than by the general practitioner. The other personal element—personality of the patient—is one of the most important elements of all. In the matter of hypnosis the will of the patient acts in just the same manner as in sleep. No one can be hypnotized without his consent, or against his will, for the early stages of the hypnotic procedure require concentration of the attention, and this implies the will of the patient. The onset of hypnotic sleep must always be willed by the patient, but after that the patient's will plays little or no part in the condition.

Technique of Hypnotization.—There have been numerous methods proposed for inducing hypnosis, but they can all be arranged in two groups: 1, Sensorial irritation; 2, direct production of sleep (suggestion). The first group includes stimulation of all sense organs—eyes, ears, skin, etc. No matter what method of sensory irritation is used, the only point to strive for is the concentration of the attention. This serves to narrow the sphere of consciousness at the start, which is essential for the onset of hypnosis. The eyes are utilized by having the patient fix his gaze on some external bright or dull object, or some part of his own or the physician's body. In the sphere of hearing the ticking of a watch, the sound of running water, and monotonous single notes, such as from a tuning fork, have a like effect. Similar results are obtained by slowly stroking some part of the body or by passing the hands in front of or over the body. In short, anything which favors the concentration of attention facilitates the onset of hypnosis. Fixation of the eyes is the oldest and still the most used method. It was used by the Yogis of ancient India

centuries ago, and their clear crystal balls, into which they gazed and foresaw events, have not, even to this day, gone out of our life. Many different objects have been used for ocular fixation—glass balls, metal buttons, lenses, coins, etc.—and all are efficacious, as the fixation is the important thing. Von Luys used a revolving mirror and Preyer a candle flame. Other authors prefer a small horseshoe magnet, while the eyes or fingers of the physician suffice others.

Stroking with the hands must be done slowly and gently in the same direction over some part of the body, preferably the face and eyes. If bodily contact is to be avoided the same result may be obtained by passing the hands near the body from the head to the hips, and then return them to the head in a wide arc. Löwenfeld uses stroking only in women and children, and always combines it with verbal suggestion. In some cases stroking retards rather than promotes hypnosis, and in others it appears to act perfectly indifferently. When it has proven efficacious, it is often all that is required to again hypnotize the patient. The use of mild auditory stimuli for hypnosis is now rather rare, if one excepts the low-toned monotonic voice one uses in talking to patients while giving the direct verbal suggestion.

Direct suggestion is the modern method and the only one which gives uniform results. Even when other methods are used, it is suggestion which we rely on for the most part. It is best always to explain to the patient exactly what you are going to do, the nature and workings of hypnosis. This is very essential in educated patients, and less so in the case of the ignorant. The explanation should be worded as simply as possible, and the patient impressed with the fact that there is nothing supernatural or mystic about the process; emphasize that it is not an experiment, but a method of cure; that his will will not be weakened, nor will it become dependent upon that of the hypnotizer. If the patient is still refractory, some physicians make a practice of hypnotizing other patients before him. While this may be efficacious, it is very seldom practical. Hypnotism is always more difficult when a third party is present, and, not infrequently, a completely hypnotized subject will immediately awaken as soon as some one else enters the room. There are, of course, instances where a witness is indispensable, such as when the patient is a girl or young woman. In this case it is frequently found best to have the third person sit in an adjoining room with the door open.

Surround the patient with all possible conditions favorable to sleep. Let him lie comfortably on a sofa, recline in an easy chair, or in any other position in which he prefers to sleep. If the patient is accustomed to taking an afternoon nap, choose that time for the hypnosis.

Practically everyone has a different method of approaching his patients, and the details of individual methods of hypnosis induction naturally differ to some degree. Each observer finds his own method the

best, so it remains for us here only to outline some of the detailed methods which have been published, which will serve as a groundwork for the development of the technique.

Bernheim's procedure is as follows: First, he explains to the patient that hypnotism can aid and cure him, and that it can have no dangerous or extraordinary effects on him; that it is simply a sleep or stuporous condition which can be produced in anyone, and that the condition results in a beneficial equilibrium of the nervous system. When necessary he hypnotizes one or two subjects before the patient to show that there is no danger; when the patient is ready, he is placed in a comfortable position, and the physician says: "Look steadily at me and think of going to sleep. Now your eyes are tired, and you begin to feel a heaviness in your eyelids. Your eyes are blinking. They are becoming moist, and you can no longer see clearly. Now your eyes are closing." In some cases this is enough to cause the eyes to close, but, if it is not successful, it may be repeated with emphasis and manipulations of some sort used. For instance, he tells the patient to look at two fingers of the physician's hands held before his eyes, or else he strokes the eyelids from above downward, still saying: "Your lids are closing; you cannot open them; your arms and legs feel weak; you hear nothing; your hands are as if paralyzed; you can no longer see; sleep comes over you; you are asleep."

As a modification of the above method, the following has been advised: The physician holds a small magnet or coin or other object in front of and just above the patient's eyes, and says: "Look closely at the magnet (coin, etc.), and think only of going to sleep." Then, with the voice becoming lower and more monotonous, he continues: "Your lids are becoming heavier and heavier; you blink; your eyes are filling with tears; your sight is getting dimmer; your eyelids sink lower and lower (here lower the object slowly), and now close; you are already sleepy and feel more and more so. Your head, your whole body, is tired; you no longer hear clearly, but as from a distance. You no longer see, you are becoming sleepier, and now you fall asleep." In most cases this is successful, but in others it must be repeated. In this method we see that the verbal suggestion is aided by two other important factors—one, fixation, and two, monotonous voice.

Löwenfeld uses a rather more elaborate technique, and one which has much to recommend it. He has his patients comfortably placed on a couch or in an easy chair, and, using eye fixation, the same as in the last-mentioned method, he talks as follows, always in a dull, monotonous tone: "Keep perfectly quiet and don't be concerned about anything else. A tired feeling, a feeling of pleasant, comfortable rest comes over you more and more. All your nerves, all your limbs, your whole body, becomes quieter and quieter; your head feels more and more tired. The tiredness extends to your eyes, and they become tired and heavy, heavier and

heavier. Your sight becomes indistinct, dim, and weak; your eyes are very tired, very heavy; your lids sink more and more, droop more and more, and now completely close (lower the fixation object while saying this). Your eyes are now closed; fatigue and sleepiness rapidly come over you. Your body becomes ever quieter and stiller; you breathe slowly and quietly; your heart beats slowly and quietly. Everything becomes quiet in your head. Thoughts become less and less; slower and slower; less and less; and the thoughts drift away from each other until your head is confused. Slumber comes over you; you slumber peacefully (lower your voice from now on). Sleepiness, drowsiness, becomes greater. You no longer think of anything; nothing concerns you; you know nothing; you see nothing; you hear only dimly and weakly. You feel nothing, you sleep ever deeper and deeper; consciousness disappears; you sleep quietly and softly, ever softly and quietly." Such a procedure of verbal suggestion is usually successful, but there are some cases in which the eyes have a tendency to open after they have been closed. In this case gentle stroking of the lids from above downward completes the hypnosis.

In analyzing this technique we see that it consists of three parts, each one of which represents a step in the hypnotizing process. The first develops fatigue and sleepiness, and so begins hypnosis. The second brings on hypnotic sleep, and the third deepens the sleep.

The modifications and variations of the above-mentioned procedures are too numerous to catalog, but one or two may be mentioned. Bernheim, often in the early stages, raises one of the patient's arms, and, placing it against the wall, says: "Your arm is stiff; see, it is not working well; your arm is becoming stiffer; you cannot lower it." When the patient tries to do so, hold it up and say rapidly: "On the contrary, when you try to bring it down, it goes up toward your head. See, I am lifting it up toward your head." In refractory cases this is often very valuable, as it tends rapidly to narrow the consciousness.

Vogt advocates what he calls a fractional method. In this hypnosis is induced in stages, for the patient is awakened occasionally to orient himself, and then the hypnosis is again started where it was left off. While Vogt claims great results for this method, and especially in obviating unpleasant results, most authors have found it less efficacious than the continuous method, and it is never to be recommended to beginners.

In very refractory cases some authors have advised that sedatives and narcotics be used in order to increase the hypnotic suggestibility. Those which have been used are morphin, bromid salts, chloral, paraldehyde, and the inhalation of small amounts of chloroform and ether. On the whole, such adjuncts are of little value, and whatever aid they may give is probably due to the autosuggestion they engender.

Autohypnosis, the ability of the patient to induce hypnosis in himself without the intervention of another, is by no means rare. It occurs most

frequently in patients who have often been hypnotized and who have become more susceptible to hypnosis each time. The hypnosis usually comes on when the patient is surrounded by some of the circumstances in which he is usually hypnotized. Those patients with whom loud noises have been used to institute hypnosis may go into the state spontaneously under similar circumstances. Kuh reports the case of a young woman whom he had frequently hypnotized by the sound of a gong. In time she became so sensitive that any loud one-toned note would immediately throw her into hypnosis. One day, while crossing the street, the sudden clanging of a church bell threw her in a state of hypnotic sleep. She was run over by a wagon and killed. Other persons have been known to hypnotize themselves by looking at bright objects, pictures, letters, telegrams, etc.

Awakening of the Patient (*Dehypnotization*).—As a general rule, this is much simpler than the original hypnotization. In most cases all that is needed is to tell the patient to awaken, but, if the hypnosis has been very deep, it may be necessary to repeat the command. When this is not successful, a thing which very seldom occurs, use any of the methods for awakening from normal sleep, such as a slap on the face, shaking the patient's arm, or calling his name. Very seldom one sees patients who, after awakening, cannot open the eyes. In this case rub the lids or blow gently on them.

If the hypnosis has not been very deep, it is not uncommon for the patients to awaken spontaneously after a few minutes to a quarter of an hour; while, in deeper hypnosis, sleep may last one or two hours. Sharp sensory irritation, such as loud noises, bright lights, etc., always awaken the patient, although he may return to sleep immediately. Internal stimuli may have the same effect, such as coughing, pain, colic, etc. Dreams, disturbing and otherwise, may also bring about the return of consciousness. Löwenfeld tells of a woman who was awakened from hypnotic sleep by dreaming of a canary singing loudly.

Not infrequently sudden awakening is followed by unpleasant effects, headache, fatigue, etc. The best way to accomplish the awakening is to tell the patient to awaken after five or ten minutes, or else say, "Wake up when I have counted three." And after a pause count up to three in a rather loud voice. When hypnosis has been used simply to get the effect of the sleep, one may say, "Wake up at the end of a half hour," or any other set time, and usually the patient will do so. The two main causes for difficulty in awakening a patient are both suggestive on the patient's part. If he has a fixed idea beforehand that he will be difficult to arouse, in all probability he will be. The other cause is autosuggestion during sleep, in that the patient's autosuggestion to remain asleep is stronger and more active than the heterosuggestion to awaken.

A final word may be spoken about the futility of violent attempts to

hypnotize resistive patients. If the attempt is not successful, do not push it until the patient is fatigued. It will not make the next attempt any easier, and it may make it impossible, as the patient may get the idea that he is not hypnotizable. Better send the patient away to return another day, when he may be in a more susceptible mood.

Normal Hypnosis

Stages.—The division of any phenomenon into stages must necessarily be more or less artificial, and vary with the individual who does the division. In hypnosis a varying number of degrees or grades of hypnosis have been described. Bernheim divides normal hypnosis into nine stages; Liebault into six; Fontans, Segard, and Forel into three; Delbœuf, Dissoir, and Hirschlaff into two. Forel's three degrees are the simplest and most easily understood, and hypnosis will be considered here from this point of view.

1. *Somnolence.* The hypnotic influence is very slight, for the patient can resist any suggestion, and also can open the eyes. 2. *Light sleep, hypolaxia, or charm.* The patient is unable to open his eyes and must accept at least a part of the suggestion offered, if not all. There is no amnesia for the hypnosis. 3. *Deep sleep or somnambulism.* This is characterized by great suggestibility, amnesia on awakening, and post-hypnotic phenomena. For ordinary therapeutic work an intermediary degree of hypnosis between stages 2 and 3 is most efficacious.

Activity of Associations.—In the state of deep hypnosis the patient appears unconscious, but in reality he is able to appreciate all kinds of sensory impulses, and to weigh them logically and understandingly. Likewise, he is capable of carrying out any mental operation which is within the capacity of his mentality when awake. The most important change that hypnosis brings about is the limiting of activity of associations. This change manifests itself in the readiness with which hypnotized patients will answer questions in great detail, telling things which, when awake, they would zealously withhold. This open-heartedness is the result of a limitation of association activity, in that all the associations which, in the waking state, would tend to cause the patient to hide a thing never enter into the hypnotized consciousness. This narrowing of the field of association also accounts for the increased suggestibility in hypnosis. When one suggests to the hypnotized patient that he is in a garden, at a theater, or in a strange city, and he sees the surroundings suggested, the basis for this credulity is the same limitation of associations which works to keep out all remonstrance. The narrowing of the mental horizon also may account for the supposed increased mental capacity in some hypnotized subjects, such as increase of mathematical accuracy, speed, etc. Gilles de la Tourette remarks that one often sees

poor, uneducated, stupid girls appear bright and lively and intelligent under hypnosis. This last observation may be due to the fact that one can bring out isolated points of a patient's life, or increase mental activity along certain lines.

The Activity of the Will.—The will is truly and actually diminished in hypnosis, and so much so that many authors have considered this decrease of will power to be the most characteristic feature of hypnosis. Mental spontaneity appears to be lacking. Whatever thoughts and acts the patient indulges in are suggested by the physician. The degree of will power lost varies in different hypnotic conditions, and does not depend simply upon the degree of hypnosis, for the personality of the patient plays a considerable rôle in the process. In somnambulism two opposite types of subject are seen. The first consists of those individuals who react actively, follow all suggestions rapidly, say and do what is wanted of them. The others are the passive cases who are apathetic, do not carry out complicated acts at all, either do not answer questions, or simply make slow lip movements. Of course, the two types depicted here are the extremes, and we see in between them many intermediary stages. Even in the lesser grades of hypnosis, the degrees of will power diminution are shown in the suggestion of automatic movements, catalepsy, and palsies. Many people who have experienced the lower grades of hypnosis say that the feature of the condition most striking to them is the inability to perform voluntary movements. These patients frequently realize perfectly the loss of will power during the hypnosis, and often they will concentrate such little will power as remains to the development of resistance to suggestion.

Suggestibility.—As has been mentioned above, increased suggestibility is one of the most characteristic features of hypnosis. The degree of suggestibility depends directly on the amount of narrowing of association activity and of diminution of will power. It has been claimed by some that the suggestibility varies directly with the depth of hypnosis, but this is not always true. It is true that most cases are more suggestible in the stages of sleep than in light hypnosis, but it is not uniform. It is possible for hypnosis to be so deep that the mind is incapable of receiving suggestive impressions. It is known that there is no relation between the ease with which a suggestion is taken during hypnosis and the duration of the suggestion after awakening (posthypnotic).

Memory.—In studying memory in hypnosis one divides it into two headings: (a) the capacity of retaining events of the present and of reproducing them after the onset of hypnosis; (b) the capacity to reproduce happenings that once were in the memory and accurately to connect them with the place and time of their occurrence. These two divisions comprise, then, the memory for the recent and for the remote past. The

memory for the recent past includes memory of events during the hypnosis and for those of a less recent past.

The memory for the remote past is sharpened to a high degree in hypnosis, but not for all events of the past. If the patient should be asked to tell what he did on a certain day, week, month, or year, no better results are obtained in hypnosis than in the waking state. Nevertheless, hypnosis is a condition of increased memory ability, for it is possible to awaken during hypnosis not only memories of normal life which have been lost to the waking consciousness, such as forgotten languages of childhood, but also those of abnormal conditions which have never existed in the memory of waking consciousness. This is done by suggestion and leading the memory back to the conditions and surroundings in which the event occurred. It is possible in this way to awaken memories of dreams and of occurrences and thoughts in hypnotic states, hysterical attacks (Dämmerzustände), and even epileptic obscurations. By suggestion also memory can be directed in different directions and patients can be made to read and write in a foreign language they once knew, to play the piano, to sew, etc. Likewise, it is possible for the memory to be caused to fail, and the patient will forget the conditions of his everyday life, that he is married, what his business is, etc.

The memory can also be falsified and patients will indulge in fabrications and romance, a fact which must be always borne in mind when one is dealing with memory aroused by hypnotic suggestion. Closely connected with this is the change of personality which suggestion can occasionally effect. Thus adults can be made to talk and act like children; a shopkeeper become a farmer; a Congressman a priest, George Washington, Napoleon, etc. With these suggested ideas accepted, the patient proceeds to act the part in great detail. Very suggestible persons may sometimes be changed to animals, dog, cat, etc., a stone pillar, or a carpet. It is very doubtful whether the patient actually believes he is the thing he pretends to be, and it is much more probable that he simply acts the part given him, as an actor does on the stage.

The retention of events during hypnosis in the waking consciousness is subject to much variation. If the hypnosis has been very deep there is usually amnesia for the hypnosis immediately after it, but at the end of a few hours or a day the memory usually returns, either completely or in part, so that the patient is confused as to the events. Again, there are cases in which the memory never returns (post-hypnotic amnesia). Bernheim has observed many patients in which the post-hypnotic amnesia includes not only the time of sleep, but also the process of hypnotization, and even some hours immediately preceding this. Post-hypnotic amnesia exists only in the waking consciousness, for when these patients are hypnotized again they can reproduce all the events of the forgotten period.

Reaction.—Many patients react only to the hypnotizer, and will accept suggestion only from him, but some patients may obey others if the hypnotizer tells them to do so. In hypnotic sleep all the senses are not dormant, as in normal sleep, but some of them remain open to the outer world and the attention is concentrated on these. Those patients who do not obey others during the hypnotic sleep nevertheless hear and understand all that is said to them, and they simply do not react to any one but the hypnotizer.

Sensations.—All sensations are preserved in light hypnosis and depressed in deep sleep to some degree, up to complete anesthesia.

Cutaneous Sensibility.—Touch, pain and temperature sense are usually diminished to some degree, and may be completely lost, and then one is able to thrust a needle through the skin. Any one of the cutaneous sensations (touch, pain, or temperature) may be caused to disappear by suggestion, and by the same means they can be accentuated. As a general rule, any suggestive anesthesia is usually accompanied by paralysis of the anesthetic part.

Sight.—Sight may be diminished even to complete blindness, both spontaneously or by suggestion, or the blindness may be but partial, either color blindness or blindness for a single person or object. In some cases the sight appears to be keener than normal, and this is probably due to autosuggestion.

Hearing.—Here the conditions are practically the same as with sight, and similar changes can be effected.

Smell.—Smell may be spontaneously lessened or lost, and the same changes may be brought about by suggestion. In other cases the sense of smell may become more acute, and the patient is able to distinguish between persons and objects wholly by the sense of smell.

The explanation of suggestive anesthesias lies in the mechanism of the perception of sensory impulses. The end organs and connecting paths are perfectly normal and functionating, but the impulses they carry never reach the narrowed consciousness of the patient, but remain rather in the subconsciousness or unconsciousness. In normal states all sensory impulses do not always reach the consciousness. This is especially true when the attention is concentrated. In hypnosis the attention can readily be concentrated on other things, and thus leave little attention left over for the impulses in the anesthetic field.

Hallucinations.—Hallucinations of many kinds may be aroused in hypnotized individuals by suggestion. The arm or leg feels intensely cold and numb following a suggestion to this effect. A ruler is mistaken for a pencil and used for such. Odorless liquids may take on exquisite or repulsive odors at the suggestion of the hypnotizer; or music may be made to come to the patient in complete silence. Frequently the suggested hallucination is not realized completely. Often a patient may be

made to accept a glass of water as a glass of beer, but at times they will state that the beer "tastes very flat."

Negative Hallucination.—By negative hallucinations is meant the inability of seeing visible objects in the visual field. This phenomenon is producible in hypnotized subjects by suggestion. If the patient is told that some present person or object is no longer there, he no longer sees it. There may be negative hallucinations in other sensory fields than that of sight. When some one is caused to drop out of the hypnotized patient's field of vision, the patient may see the chair and cushion upon which he is sitting, but not the person. This phenomenon belongs together with the suggestive anesthesias of hypnosis and the anesthesias of hysteria. In normal life negative hallucinations are frequently observed, especially during periods of great concentration. For instance, when one is greatly absorbed in a book or piece of work, it is possible for another to come into the room and even speak to the worker and have him remain ignorant of the second person's presence.

General Sensation; Impulses.—In normal hypnosis there is no spontaneous change in general feeling, but practically any change can be effected by suggestion. Pain may be diminished or increased by suggestion. Fatigue is usually felt in all hypnosis, especially toward the end, and it may be intensified or lessened by suggestive influence. Hunger, thirst, sensations of fullness and of nausea are subject to the same suggestive changes. Anxiety may be produced or allayed. Any emotion and its affect may be produced or altered, such as sorrow, anger, fear, shame, etc.

Motor Sphere.—Voluntary motion is subject to the same changes under hypnotic suggestion as we have noticed in the other spheres, namely, production, diminution, and increase. Suggestion here may be given in several ways: 1, verbal suggestion; 2, gesture; 3, making the movements beforehand for the patient to imitate. All that is necessary is for the patient to grasp the physician's meaning, it matters not by what means. Paralyses of different members can be suggested to the hypnotized subject and perfectly realized. This paralysis is usually of the flaccid variety. Catalepsy, a phenomenon in which the limbs of the patient tend to remain in any position in which they are put, is a frequent accompaniment of hypnosis. It is purely a suggestive phenomenon, and it has for its basis a decrease or loss of the power of voluntary motion. Bernheim divided hypnotic catalepsy into three types: flaccid catalepsy, flexibilitas cerea, and tetanic catalepsy. In the first type a slight force suffices to change the position of the limb; in the second a definite force is necessary to bend the catatonic limb. The resistance is easily appreciated by the observer, for it feels as though one were bending a limb made of wax; hence the name. In tetanic catalepsy the resistance is very marked, and requires great strength to be overcome. At one time it was thought that

one could judge the depth of hypnosis by the amount of catalepsy, but later this was proven to be inaccurate.

Heart, Lungs, and Temperature.—Hypnotic suggestion has been proven to be able to lessen the rate of the pulse and of respiration, but no change in the character of the pulse can be produced. Jendrassik claimed that he has been able to cause the respiration to cease for three minutes by suggestion. Krafft-Ebing has reported a case in which it was possible to cause a fall of temperature by hypnotic suggestion.

Vasomotor and Trophic Effects.—Local skin hyperemia with rise of temperature comes into the field of possibilities of hypnotic suggestion. Hemorrhages from the mucous membranes may be effected, especially epistaxis. Many authors have reported menstrual changes caused by hypnotic suggestion, in which the length of flow has been shortened and its character altered. In susceptible individuals blisters have been produced on the skin by suggestion of burning.

Secretion.—Perspiration, both local and general, can be stimulated by hypnotic suggestion, while suggestion of eating or smelling food will increase the flow of saliva, and that of smelling an onion increase the flow of tears.

Stomach and Intestines.—Practically, there is no hypnotic effect that can be produced on the digestive system. However, strong suggestion of nausea may at times occasion vomiting, and, in cases of chronic constipation, much can be done by hypnotic suggestion in establishing regular habits.

Post-Hypnotic Suggestion

Early in the study of the subject it was observed that hypnotic suggestion was not necessarily limited to the hypnotic state, but might persist for a varying length of time after the patient had awakened. This post-hypnotic suggestion occurs in two different ways. The first is when the suggestion given during hypnosis persists after the patient is awakened —continued suggestion; and the second (suggestion à l'échéance) is when a suggestion given during hypnosis is realized first after a certain time has elapsed following the hypnosis.

Most, but not all, suggestions given in hypnosis can be made post-hypnotic. The simple suggestions, such as those of cutaneous sensation (warmth, cold, anesthesia, etc.), more easily persist post-hypnotic than do the complicated ones, such as illusions and hallucinations. Suggestions which are given just before awakening are always better realized than those earlier in the hypnosis. When one considers that the suggestion must be carried out by an individual possessed more or less of his judgment and reason, it is easy to see why it is that those suggestions which have a definite end and logical reason are better realized than fantastic,

senseless ones. In the same way a suggestion to be fully realized post-hypnotic must not be too much at variance with the nature or character of the patient, or else the conscious resistance will defeat it. Thus a reputable, high-minded person cannot be caused to indulge in the lascivious or immoral. Post-hypnotic hallucinations, as a general rule, last but a few minutes, but they have persisted for hours or days.

Possibly it is an error to call these phenomena post-hypnotic, for it is not improbable that they themselves are also hypnotic, in that the patient, while realizing them, is in at least an early stage of hypnosis. Many of these patients say that, on awakening, they feel confused and restless; they feel that they must do something, and, after having done it, the unrest disappears.

Suggestion, after an elapsed period, may be realized after minutes, hours, days, or even weeks. After awakening there is complete amnesia for the matter, and the patient takes up his daily life until the appointed time arrives; then he carries out the suggestion often without knowing why he does it. The time may be appointed either directly, by naming the day and time, or indirectly, by naming the number of days and hours which are to elapse before the thing is done. Löwenfeld reports a case where, by means of post-hypnotic suggestion, the patients had been caused to break their usual routine at the appointed time. One patient was told to leave his office a quarter of an hour earlier than usual on a certain day, and go to his home in a roundabout way. Another to change the regular hour of his visit to the physician upon a certain day. Both these suggestions were carried out perfectly; but neither patient had any recollection of the suggestion, nor could they give an explanation for the break in their routine. The mechanism of this recall is probably the retention in the subconscious memory of the idea from the moment of suggestion till the appointed time, while, as far as the conscious memory is concerned, it has never existed. This assumes the possession by man of a true time sense, and it is now very probable that, in reality, we possess such a sense. As to the frequency with which post-hypnotic suggestion is possible, but little work has been done. Forel found that, out of nineteen healthy young women who had been in deep hypnotic sleep, no less than thirteen carried out post-hypnotic suggestion. Löwenfeld states that less than half of his hypnotized patients present this phenomenon.

The Utilization of Hypnotism in Medicine

In its earliest days hypnotism was put to therapeutic use in very many different diseases, for, as has been the case with every new therapeutic means, men sought in it a cure for all those chronic diseases which defy the known means of treatment.

The use of hypnotism as a method of anesthesia in major operations

was fortunately short-lived, due to the greater efficacy and ease of administration of chloroform and ether. With the increase of observations of the therapeutic working of hypnotism, its field of utility was greatly narrowed, and, at the present time, its use is restricted to the diseases of the nervous system, and mostly to the functional ones.

The therapeutic uses of hypnotism in the present day may be classified under three headings: 1, the employment of hypnotic sleep alone; 2, utilization of the increased suggestibility accompanying hypnosis; 3, utilization of the hypermnesia accompanying hypnotism.

I. Hypnotic Sleep Alone.—Hypnotic sleep without suggestion has been used by many authors, among others Obersteiner, Binswanger, Wetterstrand, and Vogt. The good results obtained are usually the same as those following natural sleep. Wetterstrand has claimed excellent results from hypnotic sleep alone, in cases of severe hysteria with prominent mental signs, and also in cases of drug habit, morphinism, cocainism, and alcoholism, and he advised long periods of sleep for his patients, lasting in some cases for weeks, and in others a month or more. Such a procedure naturally calls for the utmost care and watchfulness on the part of the attendants, and is hardly to be recommended. Vogt modified Wetterstrand's sleep by having his patients sleep for twenty hours a day, and then awaking them for food, drink, and other bodily necessities. It is self-evident that the field for this use of hypnosis must be very limited, and practically it includes only the excited states of the insane, and repeated severe hysterical convulsive attacks. It is a fact, however, that prolonged sleep for two or three hours is frequently a great adjuvant to hypnotic suggestion.

II. Hypnotic Suggestive Therapy.—Hypnotic suggestion is by far the most frequent way in which hypnotism is used in medicine at the present day. In most cases to which this mode of treatment is applicable there exists a complex of symptoms, some of which are susceptible to hypnotic suggestive influence, and others which are resistant. Many prominent symptoms are in themselves not removable by suggestion, but, when one studies the condition carefully, it will often be found to arise directly from other symptoms easily removable. Never attempt to do too much at a time, but take up the symptoms to be removed one by one, for the realization of suggested ideas always decreases in proportion to their number. In approaching such a case weigh the symptom from the following two points of view: the degree to which it is susceptible to suggestion, and the urgency for its removal. In all instances begin with the simpler points and leave the more difficult ones until later. When possible apply suggestion to the cause of the individual symptoms rather than to the symptoms themselves; for instance, when one is endeavoring to combat sleeplessness, frequently the suggestion that the patient will go to sleep at a certain hour and sleep a certain length of time is of absolutely no

avail, for there exist causes for the sleeplessness upon which the suggestion has exerted no influence, and which are more potent forces in keeping the patient awake than any contraforce of suggestion. Such causes are: heart palpitation, peculiar sensations, paresthesiæ, disturbing thoughts, etc. When the cause has been uncovered, it is often found very easy of removal by suggestion, and the resulting sleeplessness disappears.

Indirect suggestion is often more efficacious than the direct would be. This is especially noticeable in cases where pain, either local or general, is a symptom to be attacked. Frequently it is futile to tell the hypnotized patient simply that this or that pain is gone, or will go at a certain time, for the autosuggestion which forms the basis of the pain most often is the stronger of the two. If, however, the patient is given to believe that the hypnotic sleep will quiet the nerves to such an extent that the pain will leave the rested nerves, a more favorable result may be expected. Or the suggestion may be given in this fashion: "The results we get in cases like yours are very good, for pain such as you complain of does not last long; your pain, therefore, will disappear by morning."

Naturally it is to be expected that symptoms of long standing are not to be overcome at once, and the suggestion to be successful must be heightened by other means than verbal communication. When there is pain or paralysis of any member, subsidizing means greatly intensify the effect of verbal suggestion. Such means are: rubbing the affected member, baths, electricity, applications of various sorts, and indifferent drugs. These may be given either during or after the hypnosis. Repetition of the procedure in successive hypnosis likewise strengthens the suggestion and increases its efficacy.

It has been claimed that, since suggestion is the main feature of hypnotherapy, suggestion in the waking state is as efficacious as hypnotic suggestion. The experience of observers does not in the least justify this contention, for it is an established fact that many persons upon whom suggestion makes no impression while awake prove themselves to be very suggestible in the hypnotic sleep.

III. Utilization of the Increased Memory in Hypnosis.—This characteristic of hypnosis is of greater value from a diagnostic point of view than from one strictly therapeutic. There are two general ways in which this heightening of memory may be utilized by the physician; the first is to complete a history which has been too meager to orient the physician, for, in this condition of increased memory ability, events of the patient's life which have been forgotten are readily brought to the surface. This is of importance in obtaining from patients repressed and buried complexes, which play so important a part in Freud's conception of hysteria, and which will be spoken of later.

The second use that one can make of the overactive memory of hypnotism is in revealing psychic moments in the patient's life, which, for

some reason, do not exist in the patient's conscious memory. Thus one may obtain incidents which occurred during pathological amnesias, such as the hysterical and even the post-epileptic amnestic periods. Graeter, in working with an alcoholic epileptic patient who had recently gone through a period of delirium, found that, in hypnotism, the patient related with great clearness the details of the delirium and the delirious experiences.

Dangers of Hypnosis

Practically all authors agree that they have never seen any permanent untoward effects from hypnosis. Some cases, however, suffered from nervousness and headache after hypnosis, and there are others who show a tendency to autohypnosis and more or less permanent increased suggestibility. Unfortunately, it is not infrequent to observe a tendency toward autohypnotic sleep in hysterics. If possible, this must be foreseen and combated. If there exists in the patient a predisposition toward insanity, it is very probable that continued hypnotism may increase this predisposition. Precautions on the part of the physician may do a great deal toward lessening the possible bad after-effects. Do not, if possible, give suggestions which are unpleasant to the patient. Especially avoid producing hallucinations too frequently or allowing them to persist too long. Before awakening, all unnatural suggestion must be counteracted by countersuggestion. Likewise, anything which is apt to have a bad permanent effect must be first removed by suggestion.

Application of Hypnosis

It is not within the scope of this article to outline the detailed treatment of various diseases by hypnotism, but it may be permitted to mention here a few conditions in which hypnotism is advised. Forel advises it in spontaneous somnambulism, pains of all kinds, but more especially headache, neuralgias, sciatica, toothache (not due to abscess, etc.), insomnia, the functional paralyses, contractures, chlorosis, menstrual anomalies, anorexia, functional stomach disorders, constipation, nervous diarrhea, psychic impotence, nocturnal emissions, masturbation, alcoholism, morphinism, muscular and chronic articular rheumatism, neurasthenia, stuttering, blepharospasm, pavor nocturnus in children, sea sickness, vomiting in pregnancy, nocturnal enuresis (often difficult on account of normal sleep), chorea, nervous cough, hysterical attacks of all kinds, including hystero-epilepsy, anesthesia, etc. Other authors have claimed good results in dizziness, cephalalgia, depressions, chronic alcoholism, hypochondria, nervous asthma, writer's cramp, and even tabes, epilepsy, and myelitis.

As has been said before, the functional disorders of the nervous system form the most fertile field for the application of hypnotherapy, and here we see it used in the psychoneuroses, psycopathic manifestations, such as impulsive ideas and phobias, the anxiety neuroses, insomnia, tics, and sexual difficulties.

It should be borne in mind that all these functional nervous conditions are not susceptible to hypnotic influences, not to speak of cure. The more severe a case the less easily it is influenced. Hence, do not let your patient look upon it as a last hope. The idea should be firmly embedded in the patient's mind that it is a rational form of treatment and likely to make him well. This simple suggestion alone at times works wonders, for frequently the patient, for the first time in months, begins to look upon certain symptoms as unimportant. This alone may account for the good results said to have been shown in tabes and myelitis.

B. REËDUCATION

The signal success of suggestion therapy in many functional conditions and some of which at one time had been considered organic, stimulated ever-increasing interest in psychotherapeutics, and called into this field workers of many turns of mind. When, with the gradual accumulation of clinical experience, hypnotism was finally divorced from mysticism, earnest workers began to study the causes of the functional disorders of the nervous system from the standpoint of rational psychology. Thus arose reëducation therapy, which concerns itself with the eradication of the causes of neurotic symptoms through the patient's reason, rather than simply eliminating the symptoms themselves through his credulity, as we do in suggestion.

1. The Method of Dubois

Professor Paul Dubois of Berne has presented us with a system of psychotherapy which, besides its therapeutic value, gives a clear insight into the causation of psychoneuroses. Dubois had worked with Bernheim in Nancy, and was familiar with hypnotic therapy, both in theory and in its practical application. He early felt that he was not really helping his patients by hypnotism, not getting at the basis of their troubles. His sincere nature revolted at the fraud he was practicing in his appeals to the simple credulity of his patients in the artificially induced hypnotic sleep, and he endeavored to look upon the functional neuroses from the patient's point of view.

In the patient himself Dubois found the causes of the psychoneuroses.

He considered that it was not the traumatisms, illnesses, emotions, and fatigues which determine his condition, but rather his way of looking at these occurrences. The normal man, conscious of his own perfect health, resists these things with more or less voluntary indifference. The nervous patient, on the other hand, reacts abnormally to such irritants by reason of his abnormal mentality. This abnormal mentality is in large part inherited, but much also depends upon the individual's education. Mental stigmata are numerous when one considers the various forms of nervousness and the association of ideas which give rise to phobias, and foster fatal autosuggestion. Each patient reacts mentally in his own way.

Nervous patients of all kinds present a marked exaggeration of the faults of human nature. Especially are they susceptible to fatigue, sensitive and emotional to a high degree. From the standpoint of the anatomical pathologist, these patients are not sick. The autosuggestion which is the cause of most, if not all, neurasthenic symptoms is not a thing apart from the healthy man. No one is free from suggestive influences. There is none of us who is of such high mentality that his judgment and opinions are based only on reason, to the exclusion of suggestion and emotion. The judgment of every man is subject to eclipses.

The neurasthenic, however, habitually looks at things from the wrong angle. His judgment and ideas, especially those concerning his own condition, are generally hastily drawn, on insufficient grounds, from emotion and suggestion, rather than from reason. "Suggestion," says Bechterew, "enters the understanding by the back stairs, while logical persuasion knocks at the front door." Misinterpretation of bodily sensations due to autosuggestion is the most prominent feature of the psychoneuroses. Reason, the sieve which keeps unhealthy suggestion from the consciousness, is thrown away in the face of possessing fear, and the abnormal mind utilizes only its emotion and suggestibility in its reaction.

Dubois looks upon the neurasthenic and those suffering from other psychoneuroses as victims of autosuggestion. The false idea enters the mind, and there is elaborated more or less logically until, in time, the patient becomes whatever he believes himself to be; suffers whatever he thinks he will suffer. "Psychasthenia," says Dubois, "is always congenital by virtue of the heredity which outlines the characteristics of our brain."

Whoever has talked much with neurotic patients surely must feel that much of their trouble is due to the way they think, the way they interpret conditions. They all attempt to analyze their symptoms and to understand the nature of their troubles, and the mentality they bring to this task is not equal to the work. Utterly ungrounded in the physiology and pathology of the human body, they form conclusions from insufficient evidence on false premises, and in this lack of judgment we find a source of most of the unhealthy autosuggestions. Early in their disease they ac-

quire a keen faculty for self-observation, and they elaborate complete disease pictures from personal symptoms which, in normal individuals, never get beyond the subconsciousness. The pulsations of the smaller arteries, the heart-beat, the flecks in the vitreous humor, all force themselves into the patient's consciousness, and are interpreted as ominous signs which cause him anxiety and fear. Primarily they fear death, and interpret all uncommon bodily sensations as indicative of something fatal.

Dubois sees two obligations facing the physician when treating a case of what is popularly called nervousness: One, to dispel as quickly as possible the existing trouble; two, to prevent the recurrence of the disorder in the future. It is to the latter that he attached the most importance; his reëducation method consists in readjusting the patient's point of view and explaining his symptoms to him on a rational basis.

In his practice Dubois places much reliance on the Weir-Mitchell treatment of rest in bed, isolation, and overfeeding. At times he starts his patients on a preparatory milk diet, but never prolongs it longer than three days. This is especially useful in patients complaining of digestive symptoms. After this the patient should take three full meals a day, with milk three times a day between the meals. The isolation does not need to be absolute, and that depends altogether on the nature of the case.

The true reëducational parts of the treatment are the psychotherapeutic talks which the physician holds daily with patients. Great patience and forbearance on the part of the physician is essential; never hurry the patient, but rather let him take his time; encourage him to talk freely of his symptoms, and let him express everything in his own terms. In this way the physician can acquire an accurate insight into the patient's ideas, his fears, and, more important, his point of view. The study of the mental peculiarities of the patient should be made at the beginning, for the object of the treatment is to correct his mentality and right his judgment. Lead him on to describe minutely what his fears are and how he interprets the symptoms of which he complains. Have him reëstablish for you the associations with which he connected his symptoms, and have him identify as far as possible the source of the terms with which he describes them.

The neurasthenic is wont to express himself in terms of the utmost vagueness, and, not possessing sufficient accurate medical knowledge upon which to base the interpretation of his symptoms, he gladly accepts suggestions from any source, unmindful of its value. Folk lore, superstitions, casual remarks of friends, who are no more versed on the subject than he is, newspaper stories, gleanings from patent medicine advertisements, and, worst of all, medical books and the chance observations of physicians—all are of great weight in the defective judgment of the neurotic, and give him a foothold from which to jump to his hasty con-

clusion, and this conclusion, tempered by his fears, always justifies his apprehension.

The physician then must find out what the patient fears and why, and, with as much accuracy of detail as the patient has exhibited, explain to him his symptoms on a rational ground, talk to him of physiology and pathology, and show him wherein his error lies. Make him use his reason in interpreting his symptoms. Offer him a logical basis on which to build his reason. It is very essential for these patients to understand that no one is absolutely well; that minor symptoms are present in every normal man and woman, a heritage, as it were, of our years and experiences. The symptoms themselves do the neurasthenic no harm, but he suffers from his interpretation of them. He does not fear his symptoms, but rather what he believes they will lead to. This is the unhealthy autosuggestion of which Dubois speaks.

As mentioned above, a signal feature of the neurasthenic attitude is the faculty for generalizing, for arriving at broad general conclusions from isolated instances. This tendency must be combated. It frequently forms the greatest obstacle in the way of reëducation. Such a tendency is constitutional with the neurasthenic and psychasthenic, as an integral part of his nature. It is mainly because of it that he is neurasthenic. Nevertheless, it must be overcome if one is to hope for a cure. After the patient's confidence has been gained, force him to be accurate in his statements. Do not be satisfied with generalizations, but insist upon detailed statements. Never accept his explanations of his conditions unless he can prove them to you logically. When you have demonstrated the faults in his reasoning, always make it a point to point out to him the truth, and start his reasoning power on the right track.

This is the true reëducation, for it is educating the patient to think properly. Encourage him to work out his problems on a rational ground, and he is on the road to recovery. With the idea firmly fixed in the patient's mind that his symptoms do not represent as serious a condition as he had feared, the psychotherapeutist's work is practically done. "The nervous patient," says Dubois, "is on the path to recovery as soon as he has the conviction that he is going to be cured. He is cured on the day when he believes himself to be cured."

In an article such as this one cannot go into the detailed treatment of the nervous symptoms. Only general principles may be outlined. It may be remembered, in closing, that all the complaints of the neurasthenic, not due to organic causes, are amenable to this form of therapy, and the details of the method will easily suggest themselves upon the principles laid down.

2. Psychoanalyses of Freud

The psychoanalytic movement represents not only the latest and most significant contribution to psychotherapy, but it is primarily a valuable contribution to experimental psychology and to the pathology of the psychoneuroses. In the early eighties Sigmund Freud and Joseph Breuer, two Viennese physicians, began to study in detail the symptoms of a twenty-one-year-old hysterical girl, and, on the knowledge they gained of her mental processes and their relation to her symptoms, a basis was established upon which Freud later elaborated a system which is at once a school of psychology, a contribution to pathology, and a method of treatment.

It has ever been a difficult task to present fairly a subject which is still a subject of strife and no little ill feeling among scientists, and such is the position of psychoanalysis at present. For the past fifteen years it has been and still is hotly assailed by many of the leaders in psychological work, especially by the Germans, among whom it was born. It is just as stubbornly defended by an ever-increasing number of workers whose ability and sincerity demand at least respectful consideration. The discussion of such a subject belongs elsewhere rather than in an article on psychotherapy, and the author will confine himself to the merest outline of the psychoanalytic idea, and only in so far as it has a bearing on psychotherapy. It would be meaningless to describe psychoanalytical technique without a reference to its foundation, and hence the following incomplete outline of psychological mechanisms forms a necessary introduction.

Psychological Mechanisms.—*Freud* sums up his conception of hysteria in the words: "The hysteric suffers from reminiscence," but the reminiscence does not exist in the conscious life of the patient. To be more concrete, let us consider how individuals deal with strong emotional experiences which affect them unpleasantly. A young girl, for instance, experiences a sexual trauma which depresses her and causes her much mental anguish. She must needs react to it in some way or other, and this each one does according to her temperament, social position, and education. The reaction to be healthy and sufficient usually involves more or less emotional play, for it is thus that most people learn. Women have always been wont to settle their difficulties by indulging in what they call "a good cry"; thus their emotion runs its course; they have reacted to their trouble, and always "feel better" afterward. Another form of reaction is to tell their trouble to parents or other people of experience, and seek advice. The confessional has always been a valuable aid for reaction. There are some people who are able to calmly reason out the solution to a great difficulty. In every case the reaction serves one great

purpose: it firmly establishes the incident in the individual's consciousness, places it in its proper place in the memory, where, properly associated with all its contributing and surrounding circumstances, it forms a portion of the individual's experience, the basis upon which he must form his judgments and direct his conduct.

If an individual does not react, as above, to difficulties such as we are discussing, he tries to forget it, to drive it completely from his mind. Herein we have the most common of defense reactions. This forgetting of the strong emotional incidents is not by any means the passive process of allowing it to slip from the mind, to be covered over by time, but it is an active process requiring dynamic mental mechanisms.

Repression.—The first of these mechanisms Freud has termed "Repression." Whenever the incident should be recalled to the active consciousness, the individual actively represses it and drives it from the field of the things of which he is actively aware. We must consider our consciousness as consisting of two parts. It is with definite hesitancy that one attempts to divide consciousness, for no true divisions exist. The consciousness is more or less a unit, but, nevertheless, the interest is always directed on a certain part of it. In the wide range of modern life interests, we cannot possibly concentrate on everything at once. The interests, the associations, the judgments we center about our work are not the same as those of our play. They intermingle surely. One must depend, in large measure, on the other. In this way the consciousness is a unit. There are many phases also to our recreation activity; the theater, music, reading, sports, and our hobbies, each have their own individuality and occupy special interests. Our home life, our social life, our church and intellectual life, and our business life, each has its own individual associations. Hence we are always centering on only a portion of our consciousness in our activity. We are always in our waking moments keenly aware of a portion of our consciousness, while any part of the rest of it stands ready to be called to our immediate notice by association or necessity at any moment. So the two divisions of consciousness spoken of above are that part which our attention is directed upon at any given moment, which has been called "the sphere of conscious awareness," that of which we are actively aware at the time, and the whole remaining consciousness, any part of which can be brought into the sphere of awareness at any moment.

The mechanism of repression first works to keep the incident in question out of the field of awareness, and, of course, this is effected by blocking associations. As the repression becomes stronger and more associations are blocked and destroyed, the incident recedes further and further away from the field of awareness, and finally, with associations broken, it sinks from the conscious life. It does not disappear completely, however, from the memory, but exists in the unconscious memory as a more or less

isolated unassociated incident. As such it may be a source of trouble. However, it does not stay there inactive, but ever tends, by means of association, to return to the consciousness. To counteract this the individual forms resistances against it, builds around it, as it were, a resisting wall through which the individual hopes the memory of the incident cannot penetrate to reach the consciousness. Such resistance is the second step in the defense mechanism of forgetting, and is a real, active, observable process, although it may be entirely unconscious in the individual. In the case of a recent trauma, the resistances are more or less conscious and the individual realizes their existence, but later they themselves sink from the consciousness and are manifested only as character traits and in the point of view of the individual.

COMPLEXES.—When the incident has been completely submerged, it forms a "complex" which is the kernel of the *Freud* idea. The complex may consist of an incident, frequently a sexual trauma, or desires, and these are also of a sexual nature. The most persistent and frequently expressed criticism of Freud's theories is that directed toward its accentuation of the sexual as an etiological factor in neuroses. It must be borne in mind that the sexuality with which psychoanalysis concerns itself so largely is not restricted in its meaning to the gross sexual contact and its preliminaries. Its meaning is much broader than this, for it includes all that the word "love" can mean, and more, and takes in practically all the relations of the sexes with each other. From this standpoint it is not difficult to see why it plays so important a part in the life of everyone. If we are going to think of hysteria and the psychoneuroses as arising from psychological causes, why should not the sexual—the most powerful feature of our emotional life—be the most prominent? And again, in the life history of man, what has contributed more to the pleasures and also to the sorrows of the majority than the sexual, and what, according to our modern standards of civilization and religion, is more actively repressed and driven from the mind than sexual longings and incidents, especially those of grosser fiber?

Unconscious complexes and ideas are symbolized in the waking life of the patient usually in the form of symptoms. We cannot concern ourselves here with this phase of the question, for it belongs to psychopathology rather than to psychotherapy. Besides this, unconscious ideas and wishes manifest themselves most often in the average individual in dreams. Had Freud done nothing more than to have studied out dream mechanisms, his work would have been momentous. Man has always observed his dreams, wondered over them, and tried to find in them a meaning. Early philosophy held dreams to be of supernatural and prophetic nature—an idea which to-day is firmly set in the ignorant and superstitious mind. Even in this day of alleged enlightenment there is a constant demand for dream books from which the superstitious may

extract a wished-for meaning from their dreams. Dreams have their meaning, but, in searching for it, one must look into the past rather than the future.

Dream Mechanism.—Let us first consider day dreams, those satisfying reveries in which our innermost thoughts run riot. We all indulge in them to some extent, and not only do they afford us great pleasure, but they play no little part in shaping our ideas and directing our ambitions. In our day dreams we see ourselves in scenes of our own making. They are fantasies, little plays of which we always take the leading part. We picture ourselves as doing something, saying something, which is applauded by the persons whose approval we value. We are great soldiers, heroes, artists, musicians, players, authors, statesmen, or scientists, each according to his own bent. How often does the sexual creep into even the most exalted of our day dreams! In short, a day dream is a fantasy in which the dreamer pictures himself as carrying out some wish which is dear to his heart. He gratifies in his day dream an unfulfilled wish. It is in this wish fulfillment that the day dream is a source of pleasure. Freud conceived of the true dream—the night dream—as having a similar underlying cause, and the fundamental difference between the two lies in the fact that, whereas the day dream represents the fulfillment of a conscious wish, in the dream of sleep the wish is always unconscious. As the wish is unconscious and repressed, it must assume a disguise in order to get to the surface; hence, it appears in a form so changed that its true purport is not recognized. Freud sees two contents to every dream—the "manifest content," the form in which the dream is remembered by the dreamer, and the "latent content," the unconscious wish which is fulfilled. In the dreams of children the manifest and latent content are very closely related in the simple working out of the dream, while in the adult the manifest appearance of the dream is usually fantastic and its relationship to latent content is brought out only by analysis.

Freud has divided the mechanisms by which this transformation from the fundamental thought to its manifest appearance takes place into four stages, which together he calls "dream work."

1. *Condensation.*—Single elements of the manifest content seldom represent single elements of the latent content, but a number of them. Thus, figures, scenes, and incidents in dreams usually contain in them characteristics which are widely separated in the dreamer's memory, but which, nevertheless, have association connections. One sees scenes in one's dreams with settings which are wholly foreign both to the scene and to each other. Individuals who must in real life be perfect strangers to each other and to the dream environment move naturally in the setting without occasioning surprise on the part of the dreamer. Again, in our dreams, persons frequently act and speak in a manner quite foreign to their natures without our noticing the incongruity. This is due to the

condensation which crowds into the dream scenes from anywhere, and even fuses personalities in the labor of disguising the latent wish. Unrecognized persons in dreams are usually mixed persons having the appearance and characteristics of two or more individuals known to the dreamer.

2. *Displacement.*—This serves to further disguise the latent content and is manifested in the amount of attention paid to different elements in the dream. The most prominent feature in the dream as remembered usually represents an insignificant part of the latent content, while the active portions of the latent content are expressed as unessential elements in the manifest content. Likewise, the most prominent emotional effect usually accompanies the representative of the least important of dream thoughts, and vice versa.

3. *Dramatization.*—The manifest content is so arranged and systematized that each element of the latent content is represented in the manifestation. The wish is fulfilled in the dream happenings. This requires a certain sequence and purpose of the dream ideas which are grouped together in the form of a little play, comedy or drama, each part of which represents some element in the latent content. Most dreams show a tendency to portray incidents in the visual form, a characteristic which Freud has termed regression.

4. *Secondary Elaboration.*—The dream is never remembered by the conscious individual in the same form as it occurs, for in the process of apprehension by the consciousness it undergoes a process of secondary elaboration which changes its purport. This occurs both in the short period occupied by awakening and on thinking over the dream afterward. Most of the consecutiveness and rationality of dream action is the product of the secondary elaboration of the consciousness and the amount of change in form depends on the time that has elapsed between the occurrence of the dream and the telling of it. Secondary elaboration of dreams is a necessary part of the defensive repression of the consciousness, and it serves to keep whatever is unconscious and which has run riot in the dream from in this way entering the consciousness. The censor of consciousness allows the unconscious wish to enter the consciousness only when it is so changed by these mechanisms that its true purport is not recognizable. This censor acts still more effectually when it prevents dreams from being remembered at all. Everybody dreams, and those persons who deny that they ever dream are very often those in whose dreams the unconscious wish is so evident that the censor does not allow it to get by the consciousness, but actively represses it as a defensive measure.

The latent content of dreams then represents the unconscious unfulfilled wish. The manifest content may be derived from many different sources. The most frequent of these are the events of the day before and

the books read, or plays seen, before going to sleep. Any other part of the individual's experience may be called upon to supply a part of the picture by means of association. Pictures of our imagination are utilized, and even material from other dreams. Undoubtedly, also, somatic sensations may contribute to the dream picture. It is a matter of common observation how an overloaded stomach, a full bladder, cold, heat, and pain may color a dream picture.

Technique of Psychoanalysis.—From the therapeutist's point of view the aim of psychoanalytic procedure is to ascertain the nature of the unconscious complex, draw it out from the unconscious, force the patient to recognize it in its full meaning, and to reëstablish it in its proper place in his conscious memory. If one accepts Freud's theory that unconscious complexes form the basis for hysterical phenomena, it must naturally follow that, when the complex is brought from the unconscious and is firmly fixed in the consciousness, the symptoms it has occasioned must disappear. This is very frequently the case. Freud calls this "the cathartic method," for he compares it to intestinal catharsis, in that by it he removes from the patient unhealthy mental stuff which has been the cause of ill health. Likewise, the complex has been likened to an abscess—a mass of unhealthy matter surrounded by the resisting wall of leukocytes which causes definite local and general symptoms. The psychoanalytic procedure, therefore, becomes the surgeon's knife, which brings the purulent material to the light of day, removes it from the patient, makes the wall of resisting leukocytes no longer necessary, and effects a cure.

In the technique of reaching the unconscious there are four main methods: 1, the history; 2, free associations; 3, word-time association; 4, dream analysis.

1. *The History.*—The history should be taken very fully with the most minute attention to detail. Not a point should be missed. Let the patient take his time and detail all the minor points in his own words. In this way an accurate insight may be gained into the development of the disorder, the various fluctuations in its course, and their possible causes. Also frequently the stress, or lack of it, placed on certain portions of the story points clearly to the existence of possible resistances. At times a judiciously placed question will reveal a whole group of conscious and unconscious resistances, and even defensive mechanisms.

Again, the hours which the patient and physician must spend together in getting out the history serve to acquaint them with each other and to establish the physician firmly in the patient's confidence. It is hopeless to attempt any psychoanalytic work without the entire confidence of your patient, and the deeper this confidence is the surer you are of success. The ideal state is for the patient to transfer most of his interest to the physician personally, and to take such personal interest in the physician's work that he tries in every way to help (transference of libido).

Why such great confidence is necessary becomes self-evident when one reflects on the frequency with which sexual longings and experiences play a prominent part in the formation of unconscious complexes. Again, the complex represents something which the patient has been so loath to recognize, even to himself, that he has repressed it in an attempt to drive it from his being. Hence, there must exist great personal liking for the physician before the patient can state the facts, even after he recognizes them himself. Naturally, also, this excess of confidence and liking is more essential when dealing with female patients than with men, and herein lies a grave danger against which the physician must continually be on his guard.

2. *Free Associations.*—This is the method which Freud most relies upon in his psychoanalyses. The patient is placed in a comfortable position, where extreme relaxation is possible, either lying down on a couch or sitting in an easy chair, and the examiner sits either opposite him or at his head. Frequently it is well to have a monotonous sound in the room, as this tends to dull the patient's sensorium, and leaves him more free to follow up his associations. Some authors advise the use of a humming induction coil for this purpose, but at times this disturbs the patient and so defeats its purpose. The author has found that at times a rather noisy electric fan has been a great help in this direction.

Explain to the patient that you are going to give him a word to think of, and that he is to tell you everything that comes into his head while he is thinking of it—everything, no matter whether it appears ridiculous or inconsequential to the patient. Carefully follow all that the patient says, for he is sure to let slip out now and then some thought which has a definite bearing on his complexes. When a hopeful vein of thought has been struck, follow it up closely, and lead the patient on to elaborate. Prod him on with such questions as "What next?" "What are you thinking of now?" In this way forgotten periods of the patient's life of great moment are brought to light, often to the great surprise of the patient himself. In a case of complete amnesia following a severe accident, in which the amnestic period extended from a few days before the accident to the present time, the author was able, by means of free associations, to obtain from the patient all the details of the accident and the incidents which led to it with absolute accuracy, as well as many other forgotten elements. The words to be used as stimulus words in the test are obtained from the history, and also by means of the following two methods.

3. *Word-time Association.*—This method was elaborated by Jung and applied by him to psychoanalytic technique. The principle is not new, and has for years been used in experimental psychological work, and has been applied to many types of nervous diseases. Jung, however, was the first to utilize it as an indicator of emotional repression.

WORD-TIME ASSO-

Name.

	Time	Reaction	Reproduction
1 Head:			
2 Green:			
3 Water:			
4 To prick:			
5 Angel:			
6 Long:			
7 Ship:			
8 To plough:			
9 Wool:			
10 Friendly:			
11 Table:			
12 To carry:			
13 Insolent:			
14 To dance:			
15 Lake:			
16 Sick:			
17 Proud:			
18 To boil:			
19 Ink:			
20 Angry:			
21 Needle:			
22 To swim:			
23 Journey:			
24 Blue:			
25 Bread:			
26 To threaten:			
27 Rich:			
28 Lamp:			
29 Tree:			
30 To sing:			

CIATION BLANK

Date......................................

	Time	Reaction	Reproduction
31 Sympathy:			
32 Yellow:			
33 Mountain:			
34 To play:			
35 Sail:			
36 New:			
37 Custom:			
38 To ride:			
39 Wall:			
40 Stupid:			
41 Volume:			
42 To despise:			
43 Teeth:			
44 Correct:			
45 Crowd:			
46 Book:			
47 Unjust:			
48 Frog:			
49 To cut:			
50 Hunger:			
51 White:			
52 Ring:			
53 To listen:			
54 Pencil:			
55 Woods:			
56 Apple:			
57 To meet:			
58 Law:			
59 Love:			
60 Glass:			

A chart is arranged in four columns in the following order:

Stimulus word. *Reaction time.* *Reaction* *Reproduction* (see figure)

The patient is placed in a comfortable chair and the nature of the test explained to him. He is told that you will give him a word and that he is to say aloud the first thing that enters his head when he thinks of the word. The time elapsing between the giving of the word and the reaction to it by the patient is called "reaction time," and is taken with a stop-watch. Other and more accurate methods have been advised, but for practical purposes the stop-watch is amply accurate. When these points have been determined, they are put down in the proper columns, and the next stimulus word taken up in the same way. After 25 or 50 words have been recorded, go over the list again in the same order, and record the reaction to each word in the reproduction column. This time it is not necessary to record the time.

The basis of the method is this: Everyone has a normal reaction time which is not necessarily always the same, but is always normal for the individual for the time being. Ordinarily it varies from one to five seconds. When there is no underlying trouble the reaction is given in the normal time. However, when the patient is one of limited intelligence and education, the reaction time may be lengthened, because the patient either does not know the meaning of the word or else has no association connected with it. When a word is given which calls to mind something connected with the submerged complex, the phenomenon is different. Here, either because of conscious or unconscious resistances, the patient is unwilling to tell what his association is. Hence he must repress it, drive it from his mind, and then search through his memory to find another association for the word. All this takes time and the stop-watch records it. Often in such cases the reaction time is prolonged 20 or more seconds beyond the normal. This word then becomes a "significant word," and one to be used in the free association method. When the resistance and repression are very great, often the patient will declare that he is unable to think of anything with which to associate the stimulus word. In this event the word is of great significance, and it should be very closely followed up. Again, it quite frequently happens that, when the emotional repression and resistance occasioned by the word are very great, it tends to persist and disturbs the patient's attention to such an extent that the next two or three reactions are longer than normal. This does not necessarily mean that these last words have anything to do with the complex, but the long reaction time must be referred back to the truly significant word.

In the reproduction procedure the patient ordinarily gives the same or a very similar word as he did in the reaction. However, in the case of significant words, with their long reaction time, it is very common

for the reproduction to be entirely different from the reaction, and this is another evidence of the emotional repression. This is due to the same searching around in the memory to find a word which does not bear on the complex, but is associated with the stimulus word. In cases where the reaction time of words following a significant word is lengthened it is usual to have the reproduction the same as the reaction.

Freud and many others do not use the word-time association in psychoanalytic technique, as they claim it is unnecessary, and often misleading. This is undoubtedly true in the case of those adept in the technique, but, nevertheless, this method frequently proves itself of great value, especially for beginners.

4. *Dream Analysis.*—Dreams form a great wide path which leads us to the unconscious, being based, as they are, on unconscious wishes. Each dream, properly interpreted, becomes a key to the submerged wish. The patient must write out the dream as fully as possible, and as soon after it has occurred as practicable. If he will get up and write out his dream as soon as he awakens, so much the better, for we have seen in how far the secondary elaboration of consciousness changes the dream picture. In any event, insist upon the patient writing out the dream in the morning after it has occurred. After reading the dream carefully, ask the patient to explain what meaning the different parts of the dream have to him. This is best done by means of the free association method. Unconscious wishes, as we have seen, appear in dreams in symbolic form. One must determine what symbols the patient uses to express his thoughts. Many symbols have the same meaning in the dreams of many people, just as certain expressions are common in the speech of the majority, but fundamentally this symbolism is an individual matter. Symbols come from our reading, from folk lore, and, very frequently, from common quotations and slang. When the patient has explained what occurs to him when he thinks of the different expressions and incidents of his dream, the meaning of it usually becomes clear.

The following simple dream will illustrate the points mentioned above. The author does not offer this as an analysis, but simply as an example of the symbolization of the real wish meaning. A man about to leave town to visit friends in the country dreamed as follows: "I was working on construction work, as I had done in my earlier days, and seemed to have a gang of men working under me. One of them, younger than the rest, apparently a boy about 14 years of age, got tired, and asked me for a book to read. I handed him a book, and he sat down by the roadside and started to read, while I returned to work. Then I suddenly realized that in the book I had given him was a diary (which really had been destroyed years ago) which contained a complete story of my life, which I did not want anybody to know. I returned to the boy and asked

him to return me the book. He refused. I struggled with him and took it away."

Analysis of this dream revealed the following: Free associations from the boy to whom he had given something brought out a woman, the wife of the man he was to visit, who, at a previous time, had come to the patient with her troubles, which were principally of a sexual nature. He had given her advice on the matter (the book in the dream), and, in so doing, he had told her much of his own life and sexual difficulties (the diary). Afterward he had regretted this, as she was an intimate friend of the village gossip. He feared the confidence would be spread at large. The dream then meant, "I have given this woman who asked me for aid (book) the story of my life (diary), and wish I had not done so. I would like to take this knowledge from her." The patient admitted the truth of this, and stated that he would feel much easier if he could take away from the woman the knowledge of his private life which he had given her.

A word in closing concerning the use of hypnotism in psychoanalysis. In the section on hypnotism we have spoken of the use of hyperamnesia accompanying hypnosis for determining buried complexes. Freud utilized this means in his early work, but soon discarded it as unnecessary and inaccurate. It surely is unnecessary, and is to be avoided. While it is a fact that forgotten and submerged incidents may be elicited by means of hypnosis, one can never be sure of the result. The ease with which the memory may be falsified in this hypersuggestible state casts a shadow of doubt over all the information thus obtained. It not infrequently happens that the physician at first acquires a false idea of the case which only further study will clear. Under hypnosis this false idea may be suggested and the patient indulge in the recitation of pseudo-reminiscences which throw the examiner completely off the track. This falsification of memory never occurs when the free association method is used. Recently, in a case of hysteria, the author saw a patient retail pseudo-reminiscences at the suggestion of the physician to such an extent that he was thrown completely from the track of the complex.

THE CHOICE OF A METHOD

After the perusal of this all too superficial review of the various psychotherapeutic methods, the question of which to adopt must naturally occur to the reader. This question the author approaches with great reluctance, as, in his opinion, it cannot be answered definitely in the light of our present knowledge. Hypnotism has its adherents and their number is large. They see nothing in Dubois' work but the suggestion, and believe that his method is far inferior to hypnosis. Freud they refute as impossible. The Dubois school, while not as large in numbers as that

of the other, nevertheless has enthusiastic support. They look upon hypnotism as in the nature of fraud, and see in psychoanalysis useless delving in the sexual life of the patient, which is productive of as much harm as of good. The ever-growing number of psychoanalysts consider that hypnotism merely removes the upper stratum of trouble, leaving the causes untouched, while Dubois only talks certain symptoms out of his patients, and likewise does not deal with causes. They see in psychoanalysis the only true reëducation which deals with a much neglected part of our being.

How, then, is it possible, in view of these varying opinions, and with our present perspective, to give an accurate critique of the methods? Time alone and results can decide the relative merits of the procedures. However, it appears possible at present to lay down a few general principles.

Hypnotism is easy, rapid, and will produce results in many cases, but in all probability the results are not lasting. Certain cases are peculiarly susceptible to hypnotic therapy. This is especially true of the ignorant and unthinking. Reëducation requires a mentality capable of more or less intelligent coöperation, and some of our patients do not show this capability, and so are most adaptable to the suggestion of hypnotism.

It is pretty generally believed that Dubois' reëducation method is suitable to a very limited class of patients and to a still more limited class of physicians. Even more than in hypnotism, the personality of the physician plays a most important part in the cure. The amount of time required forms a drawback for some, but no psychotherapeutic procedure can be accomplished without the expenditure of much time. While it is probably true that Dubois does not strike at real causes, yet experience proves that many cases are improved, and cured, by following his methods.

Psychoanalysis undoubtedly comes nearer to original causes than either of the above methods. However, it is applicable to a rather limited class of patients. The patient must be of sufficient education to understand his mechanisms when they are explained to him, and also to coöperate in the tests. Psychoanalysis is the most time-consuming of all, for months and even years may elapse before an analysis is complete. This is a new subject, but it appears that the psychoanalytic cures are the most lasting of all. In picked cases there can be but little doubt that this is the method of choice. It is significant to remark, in passing, that many of our most enthusiastic psychoanalysts are those who have previously been adept at hypnotism, and later have adopted psychoanalysis as more valuable.

The method to use, then, depends upon the user as well as the patient. The only advice that can be given is to study your patients carefully and endeavor to adapt your psychotherapy to their needs. Reëducation—better psychoanalysis—is to be preferred to hypnotism when possible, but, in any event, fit your method to your patient, for it must be admitted that the ultimate result depends more on the patient than on the method.

C. SECONDARY AGENTS

I. Occupation and Exercises

For many years it has been recognized that patients suffering from functional nervous disorders may find health in work, but the systematic application of occupation as a therapeutic measure is not many years old. Idleness, or, better, lack of an attachment for interest, is ever prominent in the functional neuroses, and it runs hand in hand with morbid introspection. Occupation and exercises serve a purpose in drawing the patient from himself and giving him something to which to attach his interest. The indifferent neurotic, the melancholic, and the anxious neurasthenic must find something besides himself to think about, and there can be no more natural source of interest than work.

The kind of occupation chosen must depend only on the patient. In its function of stimulating interest, it must have a very personal appeal to the patient, and on this point hangs the success or failure of your occupation therapy. It would be impossible, within the scope of this article, to give the details of all occupation methods, for they are as varied as is humanity. What may appeal to one patient and lead him to health may strike in another no sympathetic note. Books have been written on the methods—basket weaving, brass hammering, cabinet work, etc., have been extolled on high; but, although of great use in many cases, they do not succeed in all. Two main principles must be adhered to if occupation therapy is to succeed. Whatever is given to the patient to do must be within his capabilities and have a definite object or purpose. As stimulation of interest and ambition is the goal at which to aim, there must be a definite reason and end attached to the occupation. If this reason and end can be something attached to the patient's home or business, just so much surer is the chance of success.

It makes very little difference to the depressed patient whether there is one fancy woven basket more or less in the world, or one stereotyped hammered brass ornament.

If, however, the patient is able to make something which could be used by himself or another, the matter immediately takes on an altogether different face. Especially is this the case when the patient is one of education. The author has seen a woman suffering from a severe depression who exhibited no interest in anything until the stockings of her two children were procured from her home and given her to darn. Here was an occupation which meant much to her, and reached the deepest spot of her nature. She learned to look forward to the weekly consignment of stockings. By this means her interests were gradually led back to her home, and she to health.

A young girl suffering from a hysterical palsy of the right arm and a deep depression was induced to crochet a bath mat for her mother. The work was carefully hidden when any of her relatives called to see her. Finally it was sent to the family, much to their surprise and the patient's pride. This stimulated her ambition to show them how much she could do, and her recovery dated from that time.

A young engineer with an anxiety neurosis resisted all attempts to arouse his interest until it was suggested to him that he make a toy automobile for his four-year-old son. The amount of time and mechanical ability he applied to this task and the joy of the child on receiving the toy led him out of himself into normal interests and health. A young business man in a depressed state found the path to health only when he spent many days in the woods, following trout streams with his pole and line.

These examples may show how important it is to emphasize the necessity of personal appeal in occupation therapy. It is never enough to force a patient to do this, that, or the other thing, but his interest must be established on the old lines of his habits. With exercises and games the same principles hold true. It is the personal appeal that counts, and the aim must be to awaken interest and ambition.

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CHAPTER XIII

NUTRITION AND DIETETICS

WARREN COLEMAN

Some knowledge of the laws of nutrition, as well as of dietetics, is requisite for the rational construction of dietaries, whether they be intended for persons in health or for those ill from disease.

Nutrition concerns the digestion and absorption of foods, the destinies and transformations of the foodstuffs after absorption, and the energy liberated within the body by their oxidation.

Dietetics, on the other hand, relates to the selection of foods that will supply a diet adequate and efficient for a given purpose with regard to the likes, dislikes, and idiosyncrasies of persons, and the methods of preparing and serving the food.

A knowledge of the fuel values of foods is likewise essential to rational feeding. The body derives energy from food in much the same manner that an engine does from coal. The universal law of the conservation of energy holds for the body as well as for the engine; that is, the body develops through oxidation a definite amount of energy from a known quantity of food. Since the total energy which the body requires for the performance of its functions is accurately known, the fuel values of all diets should be carefully adjusted to the patient's needs.

No attempt will be made to discuss here the dietetic treatment of the different diseases. For such details the reader is referred to the appropriate chapters. The purpose of this chapter is to furnish simply the information with the aid of which diets may be arranged for any disease.

FOODS

Voit (47) defines a food as a palatable mixture of foodstuffs which is capable of maintaining the body in an equilibrium of substance, or capable of bringing it to a desired condition of substance. The ideal food is a palatable mixture of foodstuffs arranged together in such proportion as to burden the organism with a minimum amount of labor (47).

Foodstuffs

Practically all of our foods, as ordinarily served, are mixtures of foodstuffs. A foodstuff is a material capable of being added to the body's substance, or one which when absorbed into the blood-stream will prevent or reduce the wasting of a necessary constituent of the organism (Lusk, 27).

Foodstuffs are classified as follows:

Proteins,
Carbohydrates,
Fats,
Inorganic substances,
Water.

Proteins.—Proteins are contained in both animal and vegetable tissues. They comprise myosin, egg-albumin, casein, gluten, gelatin, etc.

Fats.—Fats likewise are of both animal and vegetable origin. They consist for the most part of neutral fats or the glycerin esters of the higher fatty acids. In addition to fats, foods contain various complex fat-like substances which are probably of much importance in nutrition. Lecithin is a well-known representative of these substances.

Carbohydrates.—Carbohydrates are divided into *monosaccharids,* such as dextrose and levulose; *disaccharids,* such as cane-sugar, lactose, and maltose; and *polysaccharids,* such as starch, dextrin, cellulose, and glycogen.

Inorganic Substances.—Inorganic substances are represented by salts of sodium, potassium, calcium, and magnesium; chlorin, sulphur, phosphorus, iron, and iodin.

Uses of Food

The chief uses of food are: (1) To form the material of the body and repair its wastes; (2) to furnish energy for muscular and other work which the body has to do and to yield heat to keep the body warm (Atwater, 1). In forming the tissues and fluids of the body the food serves as building material. In yielding energy and heat it serves as fuel.

Uses of Proteins.—The protein of the food fulfils both of the above functions. It is the only foodstuff, however, which is capable of supplying the body with material for the building and repair of its tissue. Death follows deprivation of protein. Animal and vegetable proteins appear to be equally serviceable as building material.

As a source of energy, protein in the amounts recommended by Voit and by Atwater represents from 16-20 per cent. of the total metabolism.

It furnishes a much higher proportion of the total energy in carnivorous animals, but even they receive fat and small amounts of glycogen in their food.

The protein molecule contains a carbonaceous group which is split off and oxidized, like carbohydrate, to carbon dioxid and water, or, as in diabetes mellitus, is excreted in the urine as sugar.

When an excess of protein over the daily needs is consumed, its nitrogen is split off and rapidly excreted, chiefly in the form of urea. Nitrogenous substances are retained in the body, however, during the period of growth and during convalescence from wasting diseases.

Gelatin.—Gelatin, though a protein, cannot supply material for the building and repair of the body, but Murlin (32) has shown that it may constitute two-thirds of the daily protein ration, provided carbohydrate is liberally supplied, without detriment to health. Gelatin is a better sparer of the body protein than either carbohydrate or fat, but this fact finds only limited application in dietetics because of the difficulty of giving sufficient gelatin for the purpose. Gelatin ranks with other proteins in value as an energy-producer.

Extractives.—When meat is boiled in water, it loses, in addition to salts, various nitrogenous compounds, to which the flavor of the meat is due. These compounds are called extractives. Though they contain nitrogen, extractives cannot serve the body as building material, and they yield little, if any, energy. Extractives subserve, however, two important functions: they give flavor to meat and thus arouse the appetite, and they remove muscular fatigue and on this account are called stimulants.

Uses of Carbohydrates.—Carbohydrates are the chief source of the body's energy, whether expressed in the form of muscular work or in the form of heat. The carbohydrate of the food is transformed into glycogen and stored, principally in the liver and muscles, until needed. An excess of carbohydrate over the daily needs leads to more complete filling of the glycogen depots, or it is transformed into and stored as fat. The body has not, however, an unlimited tolerance for carbohydrate. If too much be taken, sugar appears in the urine, producing alimentary glycosuria. This is especially true for sugars. It has been stated that no amount of starch in the food can cause glycosuria, except in diabetics or those predisposed to the disease, because of its slow rate of absorption.

Another function which carbohydrate serves is to spare protein. When neither carbohydrate nor fat is available, as in the late stages of starvation, practically all of the energy is derived from protein. If protein and carbohydrate alone or protein and fat alone be given to an animal, less protein is destroyed with a liberal supply of carbohydrate than a liberal supply of fat. Rubner (36) succeeded in reducing the nitrogen output of a starving man one-half by giving carbohydrate. Carbohydrate is therefore called a sparer of protein, and it is evident that carbohydrate

is a better sparer of protein than fat. But if both carbohydrate and fat be given, in addition to protein, they appear to be dynamically equivalent, calory for calory. Landergren (23) found that a diet furnishing one-half of its calories as fat and one-half as carbohydrate protects protein as completely as a diet composed entirely of carbohydrate.

While carbohydrate cannot replace the protein required for the growth and repair of the cells of the body, it is probably necessary for the formation of the perfect protein molecule.

Uses of Fat.—Fat constitutes an important source of energy, and, like carbohydrate, is a sparer of protein. The fat of the food, when not needed immediately for oxidation, is deposited in the tissues of the body. The principal fat depots are the subcutaneous tissues, the liver, the peritoneum, and the tissues about the kidneys. These depots constitute a reserve supply of fat, to be called upon in time of need. The duration of life under the condition of starvation generally depends upon the quantity of fat present in the organism at the start (Lusk). The sources of the body fat are the fat of the food, which may be deposited without change, and carbohydrate, which is readily transformed into fat. It has not yet been determined whether fat can be formed, in the human body, from protein. It is likewise uncertain whether glycogen can be formed from fat.

Uses of Water.—Approximately two-thirds of the body consists of water. Water forms an integral part of practically all the tissues, and serves as a means of transporting nutrients to, and waste products from, the cells. Since water is constantly given off from the body through the kidneys, skin, lungs, and in the feces, it is evident that, to maintain the composition of the tissues, these losses must be made good. Animals die sooner of thirst than of hunger. Deprivation of water causes not only a change in the composition of the tissues, but appears to lead to the development of toxic albuminous products.

The average daily water requirement is about two liters, of which one-fourth is taken in the form of solid food. The demand for water in health varies directly with the losses, which in turn vary with the amount of exercise, the external temperature, and the character of the diet. A diet consisting largely of protein increases the desire for water. The variations in the demand for water which are occasioned by disease are seen in fevers, diabetes mellitus, and chronic interstitial nephritis.

Deprivation of water increases the destruction of protein in the majority of instances, though to a less extent in fat than in spare persons. Pavlov (33) has called attention to the diminution of the gastric and pancreatic secretions which follows a deficient intake of water. Limiting the amount of water does not increase the destruction of fat, as was formerly believed. This fact has special significance in the treatment of obesity.

Uses of Salts.—Organic life is dependent upon the presence of salts. Salts enter into the composition of living matter, and therefore are true

foods. They maintain the osmotic pressure of the tissues and fluids in which they are dissolved, and regulate the passage of water to and from the tissues. Deprivation of salts causes "salt hunger." A diet which is salt-poor, though rich in other foodstuffs, causes death. Vegetable diets increase the demand for sodium chlorid. Salts pass through the body for the most part without change. They are incapable of yielding energy, yet they have an important, though little-understood influence upon metabolism.

Auxiliary Articles of Diet

These comprise condiments, spices, and beverages.

Condiments and Spices.—While not foods in the sense that they are capable of yielding energy to the body, condiments and spices serve a useful purpose in man's diet. They exert an important influence upon the appetite and the processes of digestion. While condiments and spices are probably not necessary for the proper digestion of food in the case of persons leading active out-of-door lives, habit or the stress and excesses of life render them more or less essential to the average person. Foods which are not well seasoned are insipid and pall upon the taste, and consequently are less readily digested.

On the other hand, the excessive use of condiments may lead to disorders of digestion through overstimulation of the appetite and the consequent overeating, and to irritation of the stomach and intestine.

Beverages.—The use of beverages, like the use of condiments and spices, is almost universal among men. Ordinarily a meal not accompanied by one or more beverages is considered incomplete. The commoner beverages are coffee, tea, alcoholic drinks, cocoa, and chocolate. Coffee and tea are stimulants only, unless sugar and milk or cream are added. Under some conditions alcohol constitutes a food; some alcoholic beverages, such as beer, possess considerable food value, because of the presence of other constituents than alcohol. [There are two other views in regard to alcohol as a food; both still accepted by good authorities. The one that alcohol is a food *per se,* the other that it acts as a food because it prevents other foods from becoming oxidized, *i. e.,* it acts as a food-sparer.—Editor.] Cocoa when prepared with starch sugar and flavoring agents, usually vanilla, is called chocolate.

The Total Food Requirement

The body derives the energy required for the performance of its functions from the food, the potential energy of the food being transformed into heat and work. Without some knowledge of the food requirements in health, it will be found difficult to arrange rational dietaries for patients

suffering from disease. In health the appetite constitutes the chief guide to our needs and is in the main reliable. That it is not always so, is evidenced by the occurrence of various disorders from over- or under-indulgence in food.

Two methods have been employed to determine the daily food requirement of man, the empiric and the experimental. The empiric method consists in studying the food-habits of a large number of people in various occupations and taking the average quantities of food, and foodstuffs, consumed by each class. The experimental method consists essentially in measuring, in terms of heat, the amount of energy produced by the body under different conditions, as when at work, at rest, and on different diets. Many important facts have been obtained from studies of metabolism carried out upon the lower animals.

Our present knowledge concerning metabolism in man has been derived from both the empiric and experimental methods. The results of these studies have furnished us with what are known as standard requirements. It should be pointed out, however, that these standards are not absolute; they are simply guides, which may, and should, be varied according to the requirements of different individuals.

The total food requirement is generally expressed in calories or heat units. The term calory, unless qualified, may mean either the amount of heat necessary to raise 1 gram of water from 0° to 1° C., or 1,000 grams of water from 0° to 1° C. They are designated respectively as small and large calories. Usually the distinction is made by using an initial capital for the large calory, thus "Calory" means large calory. The term "calory," as ordinarily employed in medical literature, should be interpreted as large calory.

The body follows the general law of the conservation of energy, that is, the energy yielded by the food which is actually absorbed and oxidized, and which is manifested as heat or heat and mechanical work, corresponds with the potential energy of the different foodstuffs consumed. Therefore, it is possible to calculate the fuel value to the body of the different foodstuffs. Rubner's (35) figures are generally employed for the purpose.

1 gram of protein furnishes	4.1	calories.
1 gram of fat furnishes	9.3	"
1 gram of carbohydrate furnishes	4.1	"
1 gram of alcohol furnishes	7.0	"

The total energy requirement of an adult at *absolute rest* (that is, without voluntary movement of any kind) and *without food* is 22-26 calories per kilogram per day, or 1,540 to 1,820 calories for a man weighing 70 kilograms (154 lbs.). Patients confined to bed are never at absolute rest, however, within the meaning of the term, except during sleep or

when comatose, and the energy value of their food, except under special conditions and for brief periods, should not be permitted to fall below this minimum.

A number of circumstances may modify the demand for energy. Among the more important of these are the age, size of the individual, amount of muscular work, and disturbances of metabolism brought about by various diseases.

Age.—Metabolism is less active in old age, consequently less food is required. In childhood, on the other hand, the demand for energy per kilogram is greater than that of adults. The increased demand of the child for food is due, according to Rubner, to the relatively larger surface area of the child as compared with the adult—small bodies having proportionately a greater extent of surface than large bodies. If the demand is calculated by unit of surface area in square meters, the requirements of the child and adult are essentially the same. Other researches indicate that children require more energy than adults, not only because of the disproportion of surface area to weight, but because of an actual increase in the intensity of metabolism in childhood. A surplus over the actual demand of the child should always be given to allow for growth.

Atwater (1) gives the following factors for calculating dietaries for children:

Boy 15-16 years old requires 0.9 the food of a man at moderately active muscular work.

Boy 13-14 and girl 15-16 years old require 0.8 the food of a man at moderately active muscular work.

Boy 12 and girl 13-14 years old require 0.7 of the food of a man at moderately active muscular work.

Boy 10-11 and girl 10-12 years old require 0.6 the food of a man at moderately active muscular work.

Child 6-9 years old requires 0.5 food of a man at moderately active muscular work.

Child under two years old requires 0.3 the food of a man at moderately active muscular work.

Heubner (20) states that the energy requirement of a child in the first three months of life is 100 Calories per kilogram of body weight per day; in the second three months, 90 Calories; thereafter, 80 Calories and less per kilogram. The energy supply should not be allowed to fall below 70 Calories per kilogram.

Size.—In general, persons of large frame and build require more food than those who are small. The increase, however, corresponds to unit of surface area rather than to weight. For this reason, persons who are fat require relatively less food than those who are thin, though a fat person expends more energy in the performance of muscular work, because of the greater effort required to move his body.

Muscular Work.—The performance of muscular work is accompanied by an increase in metabolism and a greater supply of food is demanded. The increase is chiefly at the expense of fat and carbohydrate, though when they are not available protein may be consumed. Many investigations have shown the relation of muscular work to metabolism. The results can be best illustrated by the following table, arranged by Atwater (1):

FOOD CONSUMPTION OF PERSONS IN DIFFERENT CIRCUMSTANCES, AND PROPOSED DIETARY STANDARDS *a*

(Quantities per man per day.)

	Actually eaten			Digestible			Fuel Value
	Protein	Fat	Carbohydrates	Protein	Fat	Carbohydrates	
PERSONS WITH ACTIVE WORK	*Gms.*	*Gms.*	*Gms.*	*Gms.*	*Gms.*	*Gms.*	*Calories*
Rowing clubs in New England	155	177	440	143	168	427	3,955
Bicyclists in New York	186	186	651	171	177	631	5,005
Football teams in Connecticut and California	226	354	634	208	336	615	6,590
Prussian machinists	139	113	677	128	107	657	4,270
Swedish mechanics	189	110	714	174	104	693	4,590
PERSONS WITH ORDINARY WORK							
Farmers' families in eastern United States	97	130	467	89	124	453	3,415
Mechanics' families in United States	103	150	402	95	143	390	3,355
Laborers' families in large cities of United States	101	116	344	93	110	334	2,810
Laborers' families in United States (more comfortable circumstances)	120	147	534	110	140	518	3,925
Russian peasants	129	33	589	119	31	571	3,165
Swedish mechanics	134	79	523	123	75	507	3,330
PROFESSIONAL MEN							
Lawyers, teachers, etc., in United States	104	125	423	96	119	410	3,220
College clubs in United States	107	148	459	98	141	445	3,580
German physicians	131	95	327	121	90	317	2,680
Japanese professor	123	21	416	113	19	403	2,345
MEN WITH LITTLE OR NO EXERCISE							
Men (American) in respiration calorimeter	112	80	305	103	76	296	2,380
Men (German) in respiration apparatus	127	80	302	117	76	293	2,430
PERSONS IN DESTITUTE CIRCUMSTANCES							
Poor families in New York City	93	95	407	86	90	395	2,845
Laborers' families in Pittsburg, Pa.	80	95	308	74	90	299	2,400
German laborer's family	52	32	287	48	30	278	1,640
Italian mechanics	76	38	396	70	36	384	2,225

*a*Fats and carbohydrates in sufficient amounts to furnish, together with the protein, the indicated amount of energy.

FOOD CONSUMPTION OF PERSONS IN DIFFERENT CIRCUMSTANCES, AND PROPOSED DIETARY STANDARDS—Continued

	Actually eaten			Digestible			Fuel Value
	Protein	Fat	Carbohydrates	Protein	Fat	Carbohydrates	
MISCELLANEOUS	*Gms.*	*Gms.*	*Gms.*	*Gms.*	*Gms.*	*Gms.*	Calories
Negro families in Alabama and Virginia	86	145	440	79	138	427	3,395
Italian families in Chicago	103	111	391	95	105	379	2,965
French Canadians in Chicago	118	158	345	109	150	335	3,260
Bohemian families in Chicago	115	101	360	106	96	349	2,800
Inhabitants Java village, Columbian Exposition, 1893	66	19	254	61	18	246	1,450
Russian Jews in Chicago	137	103	418	126	98	405	3,135
Mexican families in New Mexico	94	71	613	86	67	595	3,460
Chinese dentist in California	115	113	289	106	107	280	2,620
Chinese laundryman in California	135	76	566	124	72	549	3,480
Chinese farm laborer in California	144	95	640	132	90	621	3,980
United States Army ration, peace	120	161	454	110	153	440	3,730
German army ration, peace	114	39	480	105	37	466	2,725
DIETARY STANDARDS							
Man at hard work (Voit)	145	100	450	133	95	437	3,270
Man at moderate work (Voit)	118	56	500	109	53	485	2,965
Man with very hard muscular work (Atwater)	175	(*a*)	(*a*)	161	(*a*)	(*a*)	5,500
Man with hard muscular work (Atwater)	150	(*a*)	(*a*)	138	(*a*)	(*a*)	4,150
Man with moderately active muscular work (Atwater)	125	(*a*)	(*a*)	115	(*a*)	(*a*)	3,400
Man with light to moderate muscular work (Atwater)	112	(*a*)	(*a*)	103	(*a*)	(*a*)	3,050
Man at "sedentary" or woman with moderately active work (Atwater)	100	(*a*)	(*a*)	92	(*a*)	(*a*)	2,700
Woman at light to moderate muscular work, or man without muscular exercise (Atwater)	90	(*a*)	(*a*)	83	(*a*)	(*a*)	2,450

The energy requirement of adults, reduced to calories per kilogram of body weight, may be summarized in the following table (Von Noorden, 46). In general, a man at nearly complete rest requires on the average one calory per kilogram per hour.

CALORIES PER KILOGRAM

Absolute rest	24-30
Ordinary rest in bed	30-34
Out of bed without work	34-40
Moderate work	40-45
Hard work	45-60

The Protein, Fat, and Carbohydrate Ratios

The relative proportions of protein, fat, and carbohydrate which should enter into the diet must be considered, as well as the total food requirement.

Protein Requirement.—The daily protein requirement is an important question in nutrition, and has been the subject of much discussion. The optimum protein ration has not yet been determined. It probably varies with different individuals and under different conditions, such as external temperature, amount of work done, etc.

It has been assumed that a healthy man under normal conditions would consume daily the amount of protein which he has found by experience to be suited to his needs. The almost universal support which has been accorded to Voit's recommendation, until recently, is essentially a recognition of this assumption. After studying the food-habits of a large number of people, Voit placed the daily protein requirement of a man at light work at 118 grams. Atwater, employing the same method, found the requirement to be 125 grams a day. But within the last fifteen years or so the correctness of the Voit and Atwater standards has been called into question, largely on the basis of experimental as contrasted with statistical studies. Probably the most important of these investigations has been carried out by Chittenden (10).[1] He believes "that the Voit and Atwater standards call for amounts of protein food far beyond the requirements of the body * * * provided the total calorific value of the food is sufficient" * * * "that the need for protein food may be fully met by a daily metabolism equal to an exchange of 0.12 grams of it per kilogram of body weight." For a man of 70 kilograms (154 lbs.), this represents 60 grams of protein a day, which is about one-half the Voit and less than half the Atwater standards. Chittenden's investigations were carried out on professional men, students, and soldiers. The case of Prof. Chittenden himself, suffering as he had for years from rheumatism, "bilious attacks," and sick headaches, falls rather into the category of disease with possible disorders of digestion or metabolism, so that an excess of protein over his minimal needs acted injuriously.

More recently Chittenden (11) has employed the statistical method on 108 healthy persons selected at random, and he states that as a group they represented the average type of vigorous manhood common to most university centers. They metabolized on an average 0.19 gram of nitrogen per kilogram of body weight, as contrasted with the 0.22 gram of the Voit standard. There is, therefore, close correspondence between Chittenden's experimental and statistical results. The statistical observations

[1] It will be assumed in the discussion of the daily protein requirement that fat and carbohydrate are supplied in sufficient amounts.

especially raise the question whether there may not be many persons whose daily protein requirement is entirely satisfied by appreciably less protein food than is called for by the Voit and Atwater standards.

Chittenden's views have met with vigorous opposition. It has been pointed out that the most progressive races of mankind consume protein in quantities approximating the Voit and Atwater standards. Benedict cites the poor whites and negroes of the South as examples of the deleterious effect of the low protein diet. Niceforo calls attention to the sociological status of the laborers of southern Italy, and thinks it due to the small amount of protein in their diet. McCay (30) has shown that the Bengalis, who are inferior in physical development to the Anglo-Indians and Eurasians, metabolize only about 37 grams of protein a day, or 0.11 gram nitrogen per kilogram of body weight. But it cannot yet be assumed that the relation of cause and effect in these cases has been established.

Experiments upon the lower animals indicate that the injurious effects of a low protein diet may not manifest themselves for a year or more, and while it does not necessarily follow that similar injurious effects may be caused in man, yet the experiments suggest the need for caution in accepting Chittenden's conclusions. According to Lusk, there appears to be no strongly substantiated argument why that portion of mankind living in a cool climate should not follow the general custom of taking a medium amount of protein in moderate accordance with the dictates of their appetites.

Only a limited number of investigations into the protein requirement in disease have been made, and an attempt to state the requirement for different diseases would not be justified. Therefore, until the daily protein requirement both in health and disease is more definitely determined, the wisest course for physicians and others, who have control of dietaries, appears to be to follow the older standards, or at least to permit persons to gratify their desire for protein food.

Variations in the Protein Requirement.—The demand for protein varies within much narrower limits than the demands for fat and carbohydrate. An excess of protein is needed during the period of growth, and, according to Lusk, during "training," to provide for the accompanying hypertrophy of the muscles.

The demand appears to vary also with different persons of the same sociological status. It is a matter of common observation that some persons eat more meat than others, and claim that their efficiency is impaired if their usual supply is diminished. Old people, as a rule, take less protein than those in active middle life.

Though protein is not concerned directly in the production of energy for muscular work, provided the fat-carbohydrate supply is sufficient, a greater amount of protein is allowed by both the Voit and Atwater standards for occupations entailing physical exertion. No entirely satisfactory

explanation of the increased demand has been offered. Voit assumed that muscles engaged in active work must have a free supply of protein quickly available. Magnus-Levy (28) thinks that the increased consumption of protein is not the result of purposeful selection, but is incidental to the increase in the total food.

The inclination to diminish the amount of protein in hot weather and hot climates is general and finds its explanation in the high *specific dynamic action* of protein, *i. e.,* the high proportion of potential energy which is liberated as free heat and which does not take part in the vital activities of the cells.

Our knowledge of the protein requirement in pathological states is very incomplete. Large amounts of protein are often taken in diabetes mellitus and exophthalmic goiter. The belief is current that an excess of protein is required during convalescence from the acute infective diseases because of the febrile destruction of protein which occurs, but there is reason to question whether an excess is required, if, during the course of these diseases, adequate supplies of carbohydrate and fat are furnished.

Injurious Effects of an Excess of Protein.—The body does not possess, to any marked degree, the power of storing nitrogenous substances. The carbonaceous moiety of the protein molecule is split off and the excess of nitrogen is quickly eliminated, chiefly as urea. It has been stated that the increased work thus demanded of the kidneys would damage them, but proof of the statement is lacking. An excess of protein in the diet frequently causes disturbances of digestion, which may or may not be referred subjectively to the alimentary tract. It appears probable that products of protein putrefaction may be absorbed and irritate the kidneys in their elimination, producing albuminuria, and perhaps ultimately causing nephritis. Some headaches appear to be caused by disorders of protein digestion or metabolism or both—at least, persistent headaches which are not due to any other discoverable cause sometimes disappear when the protein ration is reduced to a minimum and the form of the protein is changed, *e. g.,* from meat to milk. Prof. Chittenden found that his rheumatism grew better under the influence of a low protein diet. Some forms of eczema disappear when meat is eliminated from the diet, and the total protein of the food is reduced (Johnston). It has not yet been proved whether an excess of protein is capable of causing arterial sclerosis.

The Carbohydrate-Fat Requirement.—The greater portion of the energy of the body is derived from carbohydrate and fat. Since they are to a large extent interchangeable in the diet, they may be considered together. While it is possible for men to live, and to thrive, upon a diet of protein and fat alone, as in the case of the Eskimos, or of protein and carbohydrate alone, physiologic economy makes it expedient that the diet should contain both fat and carbohydrate. In a mixed diet, carbo-

hydrate and fat possess about equal power as protein sparers. As already stated, Landergren has shown that a diet furnishing half of its calories as fat and half as carbohydrate has the same power as a protein sparer as a diet of carbohydrate alone. As a source of energy, therefore, in a mixed diet carbohydrate and fat are interchangeable in isodynamic amounts.

The relative proportions of fat and carbohydrate in the average diet are given in the Voit and Rubner[1] standards. But the proportions vary according to personal taste and the ability of the individual to digest fat. Large amounts of fat in a mixed diet are difficult to digest, due, as Pavlov has shown, to the inhibiting influence which fat exerts upon the gastric secretion.

The conditions which affect the carbohydrate-fat demand in health are essentially the same as those which modify the total requirement of energy, and have already been considered under the "Total Food Requirement." It may be added, however, that the amount of fat consumed is generally less in hot climates and in hot weather. The reason popularly assigned is that fat is "heating." Rubner has shown that a greater amount of free heat is liberated during the metabolism of fat than during the metabolism of carbohydrates. Physicians generally advise patients who are taking fat medicinally, *e. g.,* codliver oil, to discontinue it in hot weather. Negroes form an exception to the rule that peoples living in warm climates eat little fat. They enjoy and consume fat in relatively large quantities.

Too little is known concerning the fat requirement in various diseases to justify specific recommendations. The fat in the food is increased when it is desired to have a patient put on flesh. Fat appears to possess, along with carbohydrates, the power of diminishing the febrile destruction of protein.

The Injurious Effects of an Excess of Fat.[2]—The tolerance for fat, both as regards quantity and kind, varies in health. Many persons cannot take much fat, or certain fats, without experiencing a feeling of disgust which may amount to nausea. In addition, fat is capable of producing certain well-defined local disturbances of the alimentary tract, which may be confined to the stomach or to the intestines. The commoner disorders are loss of appetite, nausea after taking food, and vomiting. These effects are probably due to the inhibitory action of fat upon the gastric secretion, or to the delay which it causes in the passage of the chyme into the duodenum. Regurgitation of the duodenal contents into the stomach sometimes occurs, and is usually followed by vomiting. An excess of fat often causes diarrhea.

[1] See Table on p. 613.

[2] The phrase "excess of fat" must be understood to relate to the tolerance of the individual rather than to the total amount of fat consumed.

Besides these local actions, an excess of fat is believed by many authorities to cause disorders of metabolism. Persons otherwise in perfect health sometimes develop acne when the food contains much fat, but whether this results from a disturbance of metabolism, or of digestion, is not known.

It has been asserted that an excess of fat is of itself capable of causing acidosis, but such a general assertion must be accepted with reserve. Deprivation of carbohydrate is followed by acidosis in disease as well as in health because of the increased demand for energy which falls upon fat, and its consequent incomplete combustion. Acidosis of this character has been observed to disappear spontaneously, and always disappears in healthy persons, upon the addition of carbohydrate to the diet. The influence of starvation upon the development of acidosis has sometimes been overlooked, and the condition has been attributed erroneously to the fat of the food or to the effect of the disease itself. For example, doubt has been cast upon the causative relation of fat to the "cyclic" vomiting of children. Magnus-Levy (29) has pointed out that the cause of acidosis in diabetes mellitus is not the fat of the food, but the preëxisting disorder of metabolism. Fat in amounts up to 250 grams a day does not cause acidosis in typhoid fever.

Czerny and Steinitz (13) believe that the majority of cases of acidosis in children are due to an excess of fat. In experiments made upon children by Czerny and Keller (12), fat was the only foodstuff which increased the ammonia excretion in the urine. Steinitz (41) has advanced the theory that the development of acidosis with fatty acid stools in the gastrointestinal disorders of children, especially the chronic forms, is due to the loss of fixed alkalis through the intestine, either in their own form or in combination with fatty acids, i. e., as soaps. Bahrdt (4) considers that the increase of alkali in the stools is due to the stimulating influence of fat upon the pancreas and the intestinal secretions; that there is not enough fatty acid present to account for all of the bases. According to Freund (15), there are but few tenable arguments and no absolutely certain metabolic-chemical facts to support the clinical impression of a causative relation between fat and acidosis. Yet for the present it seems advisable to be guided by clinical experience, and to withhold fat, or give it with caution, in the gastrointestinal disorders of children.

The generally accepted ratios of protein, carbohydrate, and fat for persons at light, moderately hard, and hard work are contained in the following table:

STANDARD RATIONS

	Voit.	Rubner.	Atwater.
Light Work.			
Protein, grams	....	123	100
Fat, grams	....	46	....[1]
Carbohydrate, grams	....	377	....[1]
Calories	....	2,445	2,700
Moderately Hard Work.			
Protein, grams	118	127	125
Fat, grams	56	52	....[1]
Carbohydrate, grams	500	509	....[1]
Calories	3,055	2,968	3,400
Hard Work.			
Protein, grams	145	165	150
Fat, grams	100	70	....[1]
Carbohydrate, grams	500	565	....[1]
Calories	3,574	3,362	4,150

Method of Reckoning the Protein, Fat and Carbohydrate Ratios for Diets of Definite Energy Values.—In Voit's standard diet for a man at moderately hard work, approximately 16 per cent. of the energy is furnished by protein, 18 per cent. by fat, and 66 per cent. by carbohydrate. With the total energy value of the diet as 3,000 calories, the calculation is made as follows:

$$16\% \text{ of } 3{,}000 = \frac{480}{4.1} = 115 \text{ grams protein.}$$

$$18\% \text{ of } 3{,}000 = \frac{540}{9.3} = 57 \text{ grams fat.}$$

$$66\% \text{ of } 3{,}000 = \frac{19.80}{4.1} = 483 \text{ grams carbohydrate.}$$

By the employment of this method, the ratios may be determined for diets of any given energy value.

[1] Fat and carbohydrate must be supplied in sufficient quantities to make up the necessary energy.

The Composition of Foods

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbo-hydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
	%	%	%	*Calories*	*Calories*	*Grams*
ANIMAL FOOD						
Beef, Fresh						
Loin, lean, E.P.[1]	13.0—24.0	11.0—15.0	......	900	199	52.5
Loin, medium fat	11.0—22.0	16.0—24.0	......	1,190	262	38.2
Loin, fat	16.0—19.0	25.0—30.0	......	1,490	329	30.4
Loin, average	19.0	19.1	......	1,155	254	39.4
Loin, porterhouse steak	21.9	20.4	......	1,270	270	37.0
Loin, sirloin steak	18.9	18.5	......	1,130	250	40.0
Loin, tenderloin	12.0—18.0	17.0—30.0	......	1,330	290	34.5
Ribs, lean	16.0—21.0	10.0—14.0	......	870	190	52.6
Ribs, medium fat	16.0—19.0	18.0—33.0	......	1,450	320	31.2
Ribs, fat	12.0—17.0	34.0—37.0	......	1,780	390	25.6
Ribs, average	17.8	24.6	......	1,370	300	33.4
Rump, lean	17.0—23.0	10.0—18.0	......	965	210	47.6
Rump, medium fat	16.0—19.0	20.0—30.0	......	1,400	310	32.3
Rump, fat	15.0—23.0	33.0—39.0	......	1,820	400	25.0
Rump, average	18.7	23.1	......	1,325	290	34.5
Beef liver	18.0—23.0	3.0—6.0	1.0—3.5	605	135	74.0
Beef marrow	2.2	92.8	......	3,955	870	11.5
Beef tongue	17.0—22.0	1.0—18.0	......	740	165	60.6
Veal, Fresh						
Leg, lean	20.0—23.0	1.0—6.0	......	570	125	80.0
Leg, medium fat	18.0—21.0	7.0—12.0	......	755	165	60.6
Loin, lean	19.0—21.0	5.0—7.0	......	615	135	74.1
Loin, medium fat	18.0—20.0	10.0—13.0	......	825	180	55.6
Loin, fat	18.0—19.0	18.0—19.0	......	1,145	250	40.0
Loin, average	19.9	10.0	......	790	175	57.2
Rib, medium fat	20.0—22.0	3.0—9.0	......	640	140	71.4
Rib, fat	16.0—20.0	11.0—31.0	......	1,160	260	38.4
Veal kidney, average	16.9	6.4	......	585	130	77.0
Veal liver, average	19.0	5.3	......	575	125	80.0
Lamb, Fresh						
Leg	15.0—18.0	15.0—27.0	......	1,300	290	34.5
Loin	17.0—20.0	25.0—35.0	......	1,540	340	29.4
Mutton, Fresh						
Leg, lean	19.0—20.0	12.0—13.0	......	890	195	51.3
Leg, medium fat	17.0—19.0	15.0—22.0	......	1,105	240	41.7
Leg, average	18.7	17.5	......	1,085	240	41.7
Loin, medium fat	14.0—20.0	26.0—38.0	......	1,695	375	26.7
Loin, free fat removed	23.7	18.5	......	1,225	270	37.0
Kidney	16.5	3.2	......	440	97	103.0
Liver, average	23.1	9.0	5.0	905	200	50.0
Pork, Fresh						
Chops, medium fat	14.0—19.0	25.0—35.0	......	1,580	350	28.6
Chops, fat	11.0—19.0	39.0—49.0	......	2,145	470	21.6
Ham, smoked, lean	19.0—20.0	17.0—24.0	......	1,245	280	35.7
Ham, smoked, medium fat	12.0—23.0	30.0—45.0	......	1,940	430	23.6
Ham, smoked, fat	12.0—19.0	42.0—57.0	......	2,485	550	18.2
Ham, smoked, average	16.5	38.8	......	1,945	430	23.6
Bacon, medium fat	6.0—18.0	57.0—80.0	......	3,030	670	14.9

[1] Edible Portion.

The Composition of Foods—Continued

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbo-hydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
ANIMAL FOOD—Cont.	%	%	%	*Calories*	*Calories*	*Grams*
Sausages						
Bologna	15.0—21.0	11.0—24.0	0.2—0.5	1,095	240	41.7
Frankfort	15.0—27.0	15.0—26.0	2.0—8.6	1,170	260	38.5
Pork	7.0—19.0	28.0—57.0	0.0—8.6	2,125	470	21.6
Poultry, etc., Fresh						
Chicken, broilers	19.0—25.0	2.0— 4.0	......	505	110	91.1
Fowls	15.0—22.0	10.0—28.0	......	1,045	230	43.5
Turkey	19.0—25.0	9.0—31.0	......	1,360	300	33.4
Chicken liver	22.4	4.2	2.4	640	140	71.4
Fish, Fresh						
Bass, black, average	20.6	1.7	......	455	100	100.0
Bass, striped, average	18.6	2.8	......	465	105	95.2
Bluefish	19.4	1.2	......	410	91	109.9
Cod	15.0—18.0	0.3— 0.5	......	325	72	138.9
Halibut steaks, average	18.6	5.2	......	565	125	80.0
Mackerel	17.0—19.0	2.0—16.0	......	645	140	71.4
Salmon, average	22.0	12.8	......	950	210	47.7
Shad, average	18.8	9.5	......	750	165	60.6
Shad, roe	20.9	3.8	2.6	600	135	74.1
Fish, Preserved and Canned						
Cod, salt, boneless, average	27.3	0.3	......	490	110	90.9
Mackerel, salt, boneless, average	17.3	26.4	......	1,435	320	31.2
Sardines	23.0	19.7	......	1,260	280	35.7
Caviare	30.0	19.7	......	1,530	340	29.4
Shellfish, etc., Fresh						
Clams	8.0— 9.0	1.0— 1.2	1.0— 2.0	240	53	189.0
Lobsters	12.0—25.0	1.0— 2.0	0.0— 1.0	390	86	116.2
Oysters	4.0—10.0	0.6— 7.0	2.0— 7.0	235	52	192.2
Scallops, average	14.8	0.1	3.4	345	76	131.5
Crabs	16.6	2.0	1.2	415	92	108.6
Meats, Cooked						
Beef, roast	15.0—29.0	20.0—41.0	......	1,620	360	27.8
Beef, round steak, roasted	19.0—34.0	3.0—17.0	......	840	185	54.1
Loin steak, tenderloin, broiled	20.0—27.0	12.0—36.0	......	1,300	290	34.5
Corned beef, canned	21.0—35.0	12.0—31.0	......	1,280	280	35.7
Tongue, canned	11.0—23.0	16.0—33.0	......	1,340	300	33.3
Lamb, Cooked						
Chops, broiled	19.0—25.0	24.0—35.0	......	1,665	370	27.1
Leg, roast	19.7	12.7	......	900	200	50.0
Mutton, Cooked						
Leg, roast	23.0—28.0	20.0—25.0	......	1,420	310	32.3
Pork, Cooked						
Ham, roast	18.0—26.0	17.0—24.0	......	1,210	281	35.6
Ham, smoked, boiled	18.0—22.0	8.0—37.0	......	1,320	290	34.5
Ham, smoked, fried	22.2	33.2	......	1,815	400	25.0
Ham, luncheon, cooked	22.5	21.0	......	1,305	290	34.5

THE COMPOSITION OF FOODS—Continued

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbohydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
	%	%	%	*Calories*	*Calories*	*Grams*
ANIMAL FOOD—Cont.						
Poultry, Cooked						
Capon	27.0	11.5	......	985	220	45.5
Chicken, fricasseed	17.6	11.5	2.4	855	190	52.6
Turkey, roast	27.8	18.4	......	1,295	290	34.5
Fish, Cooked						
Bluefish, cooked	25.9	4.5	......	670	150	66.6
Spanish mackerel, broiled	23.7	6.5	......	655	145	69.0
Dairy Products						
Eggs, hen's, raw, E. P.	11.6—16.0	8.6—15.1	......	720	160	62.5
Eggs, hen's, boiled	10.0—15.6	9.1—14.7	......	765	170	58.8
Eggs, hen's, average	13.3	11.2	......	742	165	60.6
Eggs, boiled, whites	11.6—14.8	0.0— 0.3	......	250	55	182.0
Eggs, boiled, yolks	15.3—16.8	32.2—34.4	......	1,705	380	26.3
Butter	1.0	85.0	......	3,605	800	12.5
Milk, buttermilk	3.0	0.5	4.8	165	36	278.0
Cheese, American	28.8	35.9	0.3	2,055	450	22.2
Cheese, Cheddar	27.7	36.8	4.1	2,145	470	21.3
Cheese, Cottage	16.0—26.0	0.4— 1.6	3.7— 4.9	510	115	87.0
Cheese, Dutch	30.0—45.0	16.0—19.0	......	1,435	320	31.2
Cheese, full cream	18.0—37.0	24.0—45.0	1.2— 4.0	1,950	430	23.2
Cheese, Swiss	26.0—29.0	33.0—37.0	0.9— 1.7	2,010	440	22.7
Koumys	2.6— 3.0	1.7— 2.4	5.1— 5.9	240	53	189.0
Milk, sweetened, condensed	6.0—10.0	0.4—10.6	44.0—57.0	1,520	340	29.4
Milk, unsweetened, condensed, (evaporated milk)	8.0—10.0	8.0—10.0	10.0—12.0	780	170	58.8
Milk, skimmed	3.4	0.3	5.1	170	38	263.0
Milk, whole	3.3	4.0	5.0	325	72	138.9
Whey	1.0	0.3	5.0	125	28	357.0
Woman's milk[1]	2.01	3.74	6.37	310	68	147.1
Goat's milk[1]	3.76	4.07	4.64	315	69	144.0
Cream[1]	2.5	18.5	4.5	935	206	48.6
Cream, very rich, centrifugal[2]	2.2	40.0	3.0	1,780	393	25.4
Cream, ordinary, centrifugal[2]	3.0	20.0	3.9	925	204	49.1
Cream, ordinary, gravity[2]	3.0— 3.2	16.0—20.0	3.9— 4.0	890	196	51.0
Milk, ordinary, whole[2]	3.5	4.0	4.5	320	70	143.0
Top from one quart of whole milk[2]:						
Top 16 oz. or upper one-half	3.4	7.0	4.5	440	98	100.2
Top 11 oz. or upper one-third	3.3	10.0	4.3	560	124	80.7
Top 8 oz. or upper one-fourth	3.3	13.0	4.2	670	148	67.6
Top 6 oz. or upper one-fifth	3.2	16.0	4.0	805	178	56.2
Whey from whole milk[1]	0.94	0.96	5.5	115	25	400.0
Whey from fat-free milk[3]	1.17	0.04	5.4	120	27	370.5
Matzoon or Zoolak[2]	3.5	3.5	3.7	280	62	161.2
Gelatin	89.0—97.0	......	......	1,705	380	26.3
Calf's foot jelly	4.3	......	17.4	405	90	111.1
Lard, refined	......	100.0	......	4,220	930	10.7
Lard, unrefined	2.0— 3.0	92.0—96.0	......	4,010	890	11.2

[1] From U. S. Dept. of Agriculture Farmers' Bulletin No. 363.
[2] From Holt, "The Diseases of Infancy and Childhood," New York, 1904.
[3] From Analyses by Adriance.

THE COMPOSITION OF FOODS—Continued

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbo-hydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
	%	%	%	*Calories*	*Calories*	*Grams*
ANIMAL FOOD—Cont.						
Dairy Products						
Oleomargarine	1.2	83.0	......	3,525	780	12.8
Beef-juice	4.9	0.6	......	115	25	400.0
VEGETABLE FOOD						
Barley, meal and flour	9.0—13.0	1.5— 3.2	70.0—74.0	1,640	360	27.8
Barley, pearled	7.0—10.0	0.7— 1.5	77.0—78.0	1,650	360	27.8
Barley water[1]	0.09	0.05	1.6	36	8	1250.0
Buckwheat flour	4.0—10.0	0.5— 2.3	71.0—81.0	1,620	360	27.8
Buckwheat preparations, farina, and groats, average	10.9	0.4	84.0	1,660	370	27.1
Corn-meal, unbolted	8.0— 9.0	4.5— 5.2	72.0—75.0	1,730	380	26.3
Corn-flour	6.0— 8.0	1.0— 2.0	77.0—80.0	1,645	360	27.8
Corn-meal, granular	7.0—12.0	1.0— 5.0	68.0—80.0	1,655	370	27.1
Hominy, raw	6.0— 9.0	0.2— 1.0	77.0—81.0	1,650	360	27.8
Hominy, cooked	2.2	0.2	17.8	380	84	119.0
Oatmeal, raw	13.0—21.0	6.0— 9.0	64.0—70.0	1,860	410	24.4
Oatmeal, boiled	2.8	0.5	11.5	285	63	159.0
Oatmeal, gruel	0.9— 1.6	0.2— 0.5	3.0—10.0	155	34	294.0
Oatmeal water	0.4— 0.9	0.0— 0.1	1.3— 4.5	70	15	666.6
Rice	5.9—11.3	0.1— 0.7	75.4—81.9	1,630	360	27.8
Rice, boiled	1.6— 5.0	0.0— 0.1	15.5—41.9	510	115	86.9
Rye flour	4.9— 8.8	0.2— 1.3	77.6—80.2	1,630	360	27.8
Wheat flour	12.2—14.6	2.1— 1.5	69.5—77.0	1,675	370	27.1
Wheat flour, patent roller process	8.4—14.7	0.3— 1.6	70.3—80.0	1,660	370	27.1
Farina	10.4—11.7	0.8— 3.8	74.6—78.5	1,685	370	27.1
Shredded wheat	9.6—11.4	1.3— 1.6	75.0—79.7	1,700	380	26.3
Macaroni	7.9—16.6	0.0— 4.9	67.2—78.4	1,665	370	27.1
Bread, brown, as purchased	5.0— 5.8	1.2— 2.4	43.6—50.7	1,050	230	43.5
Bread, corn (johnny cake)	6.5—10.1	2.3— 9.8	40.3—54.3	1,205	280	35.7
Bread, rye	6.4—11.1	0.1— 1.4	45.6—65.8	1,180	260	38.4
Bread, gluten	8.2—11.1	0.7— 2.4	44.6—53.0	1,160	260	38.4
Bread, graham	6.8—10.9	0.4— 3.8	38.6—59.1	1,210	270	37.1
Rolls, plain	8.6—11.9	0.4— 9.4	56.7—64.7	1,470	320	31.2
Rolls, all analyses, average	8.9	4.1	56.7	1,395	310	32.3
Toasted bread	10.6—12.8	0.6— 3.2	56.7—67.1	1,420	310	32.3
Bread, white, home-made	6.8—11.0	0.4— 3.5	47.6—58.0	1,225	270	37.1
Bread, white, all analyses, average	9.2	1.3	53.1	1,215	270	37.1
Bread, whole wheat	8.1—11.7	0.4— 2.7	37.2—56.2	1,140	250	40.0
Zwieback	8.6—11.7	8.1—11.3	72.1—74.2	1,970	435	23.0
Crackers, Boston, split	10.7—11.3	9.9	68.8—73.4	1,885	415	24.1
Crackers, cream	8.6—11.2	10.7—13.8	68.0—72.4	1,990	440	22.8
Crackers, graham	7.4—14.4	1.1—13.6	69.7—77.2	1,955	430	23.2
Crackers, oatmeal	10.4—13.1	8.5—13.7	68.3—69.6	1,970	435	23.0
Crackers, saltines	9.9—11.2	12.7—12.8	67.1—69.9	2,005	440	22.8
Cake, chocolate layer	6.2	8.1	64.1	1,650	365	27.5
Cake, coffee	4.9— 9.0	4.7—10.5	52.4—78.8	1,625	360	27.8
Cake, cup	5.2— 6.6	2.5—15.6	63.2—73.8	1,765	390	25.6
Cake, frosted	5.0— 7.5	7.5—10.6	58.3—71.0	1,695	375	26.7
Gingerbread	5.4— 6.3	8.4— 9.5	62.3—64.7	1,670	370	27.1
Cake, sponge	5.7— 7.3	6.4—13.0	57.3—71.1	1,795	395	25.3

[1] From Holt, "The Diseases of Infancy and Childhood," New York, 1904.

THE COMPOSITION OF FOODS—Continued

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbo-hydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
VEGETABLE FOOD—Cont.	%	%	%	*Calories*	*Calories*	*Grams*
Cake, all analyses except fruit cake, average	6.3	9.0	63.3	1,675	370	27.1
Cookies, all analyses, average	7.0	9.7	73.7	1,910	420	23.8
Ginger snaps	5.8— 7.3	2.3—15.4	71.9—80.8	1,895	420	23.8
Macaroons	3.1—10.6	9.6—21.5	57.1—71.4	1,975	435	23.0
Doughnuts	5.1— 7.6	16.4—25.7	45.8—63.2	2,000	440	22.8
Pie, apple	2.6— 3.8	7.7—11.3	40.3—46.2	1,270	280	35.7
Pie, custard	4.2	6.3	26.1	830	180	55.6
Pie, mince	4.5— 7.5	9.7—14.5	30.4—44.0	1,335	295	34.0
Pie, squash	4.4	8.4	21.7	840	185	54.1
Pudding, Indian-meal	5.5	4.8	27.5	815	180	55.6
Pudding, rice custard	4.0	4.6	31.4	825	180	55.6
Pudding, tapioca	2.8— 4.2	2.3— 4.8	21.9—38.1	720	160	62.5
Pudding, tapioca with apples	0.3	0.1	29.3	555	125	80.0
Candy	......	......	96.0	1,785	395	25.3
Honey	0.2— 1.1	......	77.3—85.4	1,590	350	28.6
Molasses	0.0— 5.1	0.0— 0.2	58.8—76.7	1,290	285	35.1
Starch, arrowroot	......	......	97.5	1,815	400	25.0
Starch, cornstarch	......	......	90.0	1,675	370	27.1
Starch, tapioca	0.2— 0.6	0.0— 3.0	86.6—89.0	1,650	365	27.5
Sugar, coffee or brown	......	......	95.0	1,765	390	25.6
Sugar, granulated	......	......	100.0	1,860	410	24.4
Sugar, maple	......	......	74.0—95.2	1,540	340	29.4
Syrup, maple	......	......	45.9—81.9	1,330	295	34.0
VEGETABLES						
Artichokes	2.2— 2.9	0.1— 0.2	15.3—18.3	365	81	123.3
Asparagus, cooked	2.1	3.3	2.2	220	49	204.0
Beans, butter, green, E. P.	9.4	0.6	29.1	740	165	60.6
Beans, dried	19.9—26.6	1.4— 3.1	57.2—63.5	1,605	355	28.1
Beans, lima, dried	12.8—24.5	0.6— 1.9	61.6—70.1	1,625	360	27.8
Beans, lima, fresh, E. P.	3.2	0.3	9.9	255	56	178.7
Beans, string, cooked, E. P.	0.8	1.1	1.9	95	21	477.0
Beans, string, fresh, E. P	1.7— 2.8	0.4	12.6	300	66	151.5
Beets, cooked, E. P.	2.3	0.1	7.4	185	41	244.0
Beets, fresh, E. P	0.9— 3.0	0.1— 0.2	3.8—16.3	215	47	216.0
Cabbage, E. P.	0.2— 2.9	0.1— 0.7	3.4— 8.0	145	42	238.0
Carrots, fresh, E. P.	0.7— 2.0	0.0— 0.7	6.5—13.8	210	46	218.0
Cauliflower	1.6— 2.0	0.2— 8.0	3.4— 6.0	140	31	323.0
Celery, E. P.	1.0— 1.4	0.1— 0.2	3.0— 4.6	85	19	526.0
Corn, green, E. P	2.8— 3.7	1.0— 1.1	14.1—22.6	470	105	95.4
Cucumbers, E. P	0.5— 0.9	0.1— 0.5	2.2— 4.0	80	18	556.0
Lentils, dried	24.5—26.6	0.7— 1.5	58.6—59.8	1,620	360	27.8
Lettuce, E. P	0.7— 1.8	0.1— 0.6	1.6— 4.9	90	20	500.0
Mushrooms	1.7— 6.0	0.2— 0.9	2.4—20.3	210	46	218.0
Onions, fresh, E. P	0.2— 4.4	0.1— 0.8	4.2—15.5	225	50	200.0
Onions, cooked, prepared	1.2	1.8	4.9	190	42	238.0
Parsnips	1.4— 1.9	0.2— 0.8	8.0—17.0	300	66	151.5
Peas, dried	20.4—28.0	0.8— 1.3	58.0—67.4	1,655	365	27.5
Peas, green, E. P	4.4— 8.0	0.3— 0.6	13.4—18.9	465	105	95.4
Peas, green, cooked	6.7	3.4	14.6	540	120	83.3
Potatoes, raw or fresh, E. P.	1.1— 3.0	0.0— 0.2	13.5—27.4	385	85	117.8
Potatoes, cooked, boiled	1.8— 3.1	0.0— 0.4	16.1—26.5	440	97	103.1
Potatoes, cooked, chips	6.0— 7.6	35.5—44.2	42.7—50.6	2,675	590	16.9

The Composition of Foods—Continued

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbo-hydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
	%	%	%	*Calories*	*Calories*	*Grams*
VEGETABLES—Cont.						
Potatoes, cooked, mashed and creamed	2.0— 3.6	1.0— 4.5	13.9—22.4	505	110	90.9
Potatoes, sweet, raw or fresh, E. P.	0.4— 3.7	0.2— 1.4	17.1—49.1	570	125	80.0
Potatoes, cooked and prepared, sweet	3.0	2.1	42.1	925	200	50.0
Sweet cassava[1]	1.1	0.2	30.2	610	135	74.1
Cassava starch[1]	0.5	0.1	88.8	1,625	360	27.8
Cassava bread[1]	9.1	0.3	79.0	1,650	365	27.4
Cassava cakes or wafers[1]	1.1	0.2	85.2	1,670	370	27.0
Taro[1]	1.8	0.2	23.2	475	105	95.3
Yams[1]	1.8	0.2	23.3	475	105	95.3
Yautia tubers[1]	2.2	0.2	26.1	535	120	83.3
Radishes, E. P.	0.5— 3.0	0.0— 0.3	3.4— 8.3	135	30	334.0
Spinach, fresh	1.8— 2.4	0.2— 0.5	3.1— 3.4	110	24	417.0
Spinach, cooked	2.1	4.1	2.6	260	57	175.4
Squash, E. P.	0.6— 3.1	0.1— 1.4	3.5—16.5	215	47	216.0
Tomatoes, fresh	0.3— 1.3	0.2— 1.4	2.2— 6.5	105	23	435.0
Turnips	0.7— 3.9	0.1— 0.4	2.8—23.8	185	41	244.0
Vegetables, Canned						
Asparagus	0.9— 2.4	0.0— 0.2	2.2— 4.1	85	19	526.0
Beans, baked	5.1— 8.1	0.3— 6.8	13.1—23.2	600	135	74.0
Beans, string	0.6— 4.0	0.0— 0.5	2.0—13.5	95	21	477.0
Beans, lima	3.2— 5.6	0.2— 0.6	10.5—17.9	360	79	126.7
Corn, green	2.0— 3.7	0.5— 1.9	9.8—25.8	455	100	100.0
Peas, green	1.6— 6.1	0.0— 0.8	4.9—17.4	255	56	178.5
Succotash	2.9— 4.4	0.7— 1.7	14.9—22.4	455	100	100.0
Tomatoes	0.3— 1.7	0.1— 0.3	1.4— 8.1	105	23	435.0
Catsup, tomato	1.1— 2.0	0.1— 0.4	8.5—16.1	265	58	172.3
Olives, green, E. P.	1.1	27.6	11.6	1,400	310	32.3
Pickles, cucumber	0.4— 0.7	0.1— 0.5	1.3— 5.4	70	15	666.6
FRUITS						
Apples	0.1— 0.8	0.1— 1.4	8.8—21.3	290	64	156.1
Apricots, E. P.	1.1	......	13.4	270	60	166.8
Bananas, yellow, E. P.	1.0— 1.6	0.0— 1.4	16.3—29.8	460	100	100.0
Blackberries	0.9— 1.5	0.5— 2.9	7.5—16.7	270	60	166.8
Cherries, E. P.	0.7— 1.1	0.8— 0.8	11.4—20.6	365	81	123.3
Cranberries	0.4— 0.5	0.4— 0.9	9.3—10.9	215	47	216.0
Grapes, E. P.	1.3	1.6	19.2	450	99	111.1
Lemons, E. P.	0.8— 1.1	0.1— 1.5	8.2— 9.0	205	45	226.0
Lemon juice	......	......	9.8	180	40	250.0
Oranges, E. P.	0.8— 1.1	0.1— 0.3	11.6—18.5	240	53	189.0
Peaches, E. P.	0.4— 0.9	0.1— 0.1	9.3— 9.4	190	42	238.0
Pears, E. P.	0.6— 0.6	0.1— 0.8	14.1—14.2	295	65	154.0
Plums, E. P., average	1.0	......	20.1	395	87	115.0
Prunes, E. P., average	0.9	......	18.9	370	82	122.0
Raspberries, red, E. P.	1.0	......	12.6	255	56	178.5
Strawberries, E. P.	0.6— 1.2	0.4— 1.1	4.4—12.3	180	40	250.0
Watermelon, E. P.	0.3— 0.6	0.1— 0.2	6.5— 6.9	140	31	323.0

[1] From Bulletin No. 295, Dept. of Agriculture.

THE COMPOSITION OF FOODS—Continued

Slightly modified from Atwater and Bryant, U. S. Dept. Agriculture, Bull. No. 28 (revised edition)

Food Materials	Protein (N. x 6.25)	Fat	Carbo-hydrates	Fuel Value per pound	Fuel Value per 100 gms.	100-Calory Portions
	%	%	%	*Calories*	*Calories*	*Grams*
Fruits, Dried						
Apples	1.2— 2.5	0.1— 5.0	48.6—86.9	1,350	300	33.4
Currants, Zante	1.0— 4.7	0.4— 4.7	60.0—85.3	1,495	330	30.3
Figs	2.6— 5.7	0.3— 0.3	68.3—83.1	1,475	325	30.8
Prunes, E. P	1.4— 3.2	......	68.1—78.6	1,400	310	32.3
Fruits, Canned, etc.						
Raisins, E. P	2.3— 3.0	0.5— 7.2	71.3—78.8	1,605	355	28.1
Apple sauce	0.2	0.8	37.2	730	160	62.5
Marmalade (orange peel)	0.6	0.1	84.5	1,585	350	28.6
Strawberries, stewed	0.7	......	24.0	460	100	100.0
NUTS						
Almonds, E. P	16.6—25.3	48.9—60.0	12.8—21.4	3,030	670	14.9
Brazil nuts, E. P	17.0	66.8	7.0	3,265	720	13.9
Chestnuts, fresh, E. P	4.1— 8.0	2.0—10.8	36.9—54.0	1,125	250	40.0
Cocoanut without milk	3.6	31.7	17.5	1,730	380	26.3
Filberts, E. P	15.6	65.3	13.0	3,290	725	13.8
Hickory nuts, E. P	15.4	67.4	11.4	3,345	740	13.5
Peanuts, E. P	19.5—29.1	32.3—48.8	15.3—40.4	2,560	565	17.7
Peanut-butter	29.3	46.5	17.1	2,825	625	16.0
Pecans, unpolished, E. P	9.6	70.5	15.3	3,435	760	13.1
Walnuts, California, black, E. P	24.9—30.3	54.7—57.8	7.4—16.1	3,105	685	14.6
MISCELLANEOUS						
Chocolate	12.5—13.4	47.1—50.2	26.8—33.8	2,860	630	15.9
Cocoa	20.6—22.7	27.1—31.5	35.3—40.6	2,320	510	19.6
Beef soup	2.7— 6.2	0.3— 0.5	0.0— 2.2	120	26	384.0
Bean soup	3.2	1.4	9.4	295	65	154.0
Chicken soup	10.5	0.8	2.4	275	61	164.0
Clam chowder	0.7— 2.9	0.5— 1.1	2.5—11.0	195	43	236.0
Meat stew	3.7— 5.6	2.0— 6.4	4.3— 7.9	370	82	122.0
Soups, Canned						
Asparagus, cream of	2.5	3.2	5.5	285	63	159.0
Bouillon	1.7— 2.6	0.0— 0.2	0.1— 0.3	50	11	909.0
Celery, cream of	2.1	2.8	5.0	250	55	182.0
Chicken gumbo	3.0— 4.6	0.2— 1.7	3.8— 5.5	195	43	236.0
Chicken soup	3.2— 3.9	0.0— 0.2	1.2— 1.7	100	22	455.0
Mock turtle	4.5— 5.9	0.5— 1.3	1.6— 3.9	185	41	244.0
Oxtail	3.9— 4.1	0.5— 2.1	4.2— 4.3	210	46	218.0
Pea soup	1.5— 5.8	0.0— 1.6	5.1—11.1	235	52	192.5
Tomato soup	1.7— 1.9	0.9— 1.2	5.3— 6.0	185	41	244.0

PERCENTAGE COMPOSITION OF TRUE AND SO-CALLED GLUTEN FLOUR

From Wiley, "Foods and Their Adulteration," Philadelphia, 1911

Name	Protein	Fat	Carbohydrates
	%	%	%
Gum glutin (Hoyt's)	31.80	1.55	54.15
Educator standard gluten flour	26.40	1.67	59.38
Gluten flour, 40 per cent	40.25	1.18	47.42
	41.10	1.10	47.90
Self-raising gluten flour, 40 per cent	38.70	1.30	50.10
Pure gluten flour	78.80	0.90	12.60
20 per cent. gluten flour	21.00	0.70	68.20
Pure gluten flour, glutosac	35.20	0.60	55.00
Gluten food	85.40	0.56	3.69
Protosac	36.60	0.86	51.03
Washed gluten flour	62.40	0.91	29.51
Glutosac	34.06	1.57	52.13
Diabetic biscuit flour	75.25	8.96	5.89
Plasmon meal	78.65	2.72	0.
Aleuronat	86.10	0.51	4.00
	73.65	0.24	14.55
Roborat	82.20	3.67	3.00
Wheat protein	84.10	1.40	4.80
Energin from rice	83.70	4.54	0.67
Vegetable gluten	61.37	1.55	28.23
Casoid flour	85.56	0.50	0.
Sanitas nut meal	29.00	51.66	12.13
Soy bean meal	39.87	19.06	25.09
Almond meal	50.62	15.63	15.90
Gluten flour	11.37	0.90	74.38
Gluten flour	15.50	2.60	70.80
Diabetic flour	12.00	0.46	76.45
Jireh diabetic flour	14.30	2.21	71.95
Special diabetic flour	14.25	2.96	67.47
Gluten flour	13.30	1.05	72.11
Gluten flour	16.40	3.15	70.60

THE EFFECTS OF COOKING UPON FOOD[1]

The practice of cooking food is universal. All existing races follow the custom, at least as regards part of their food, and archeological researches indicate that the art of cooking extended far into prehistoric times. Cooking plays an important part in the preparation of food for human consumption. Substances which in their natural state are insipid and nearly, or quite, indigestible become valuable foods when subjected to the processes of cooking.

The objects sought in the cooking of meats and vegetables are essentially similar. They are as follows:

I. To develop flavor and improve the appearance of the food.

[1] In the preparation of this section the author has derived much assistance from U. S. Dept. of Agriculture Bulls. Nos. 43, 67, and 102, and Farmers' Bulls. Nos. 34 and 389.

Foods which are attractive in appearance, of pleasant aroma, and savory taste stimulate the secretion of the "appetite juice" and thus indirectly become more digestible.

II. To increase its digestibility.

Cooking produces both physical and chemical changes in the food. It is more important in the case of vegetables than in the case of meats. Both are rendered more digestible.

In the process of cooking the connective tissue of meat is softened and in part converted to gelatin. In consequence, mastication is easier and more complete, thus insuring freer access of the digestive juices to the muscle fibers. While heat coagulates the albumins of meat, and, it is thought, renders them slightly less digestible, this effect is probably more than offset by the above-mentioned advantages, unless the meat be cooked too long.

Vegetables consist for the most part of starch, which is inclosed within cellulose walls. Cellulose is practically undigested by man, and much of the starch of raw vegetables escapes from the body in the feces. Moreover, raw starch itself is difficult of digestion. During the process of cooking, the starch grains swell, burst the cell walls, and become softer. In addition starch is converted partly to dextrin: this occurs both in moist and dry heat.

Except for the development of flavor, fats are probably affected but little by the process of cooking unless they are scorched.

III. To destroy parasites and bacteria.

When meat is taken only from healthy animals and is properly inspected, there is little danger from parasites or bacteria. But these precautions are not always followed, especially in the case of meats which are sold to the poor; therefore, meats of doubtful origin should always be thoroughly cooked.

Vegetable foods, likewise, may carry infection. The typhoid bacillus, for example, may enter the body upon green vegetables which have been washed or grown in polluted water.

The Cooking of Meats.—The various methods of cooking meats may be grouped under two headings:

1. Methods which are intended to prevent the loss of the juices of the meat, such as roasting and broiling. By these methods the meat is heated rapidly, the surface albumin coagulated, and the juices of the meat retained.

2. Methods which permit the loss of the juices, such as boiling and stewing. With these methods the meat is heated slowly, and the juices escape to a greater or lesser extent.

Losses in Cooking Meat.—Meat loses in weight whatever the method of cooking. This is due to the driving off of water, and it follows that a given weight of cooked meat holds a higher percentage of nutriment than

the same weight of raw meat. According to Grindley (16), the loss in weight amounts to $\frac{1}{5}$—$\frac{1}{3}$, whether the meat be boiled or roasted. The loss in the solids of the meat is greatest when it is boiled or stewed, and the longer it is cooked the greater the loss. The loss may reach 3-20 per cent.

While meat which is boiled gives up most of its flavor to the water and becomes insipid, it loses very little of its nutriment. It is the rich taste of beef tea which gave rise to the fallacy that it contained the nutritious elements of the meat in quantity.

Cooking Vegetables and the Losses Incurred.—Losses occur in the cooking of vegetables, which are comparable to, but perhaps not so important as, those which occur in the cooking of meats by methods which do not retain the juices. The losses in the cooking of vegetables depend largely upon the method employed, and concern chiefly the sugars and salts which are soluble in water, though nitrogen also is lost. The losses to which potatoes, carrots, and cabbage, selected as types, are subject have been studied by Snyder (39). His experiments showed the following results:

1. That in order to obtain the highest food value, potatoes should not be peeled before cooking.
2. When peeled, the least loss occurs if the potatoes are put directly into boiling water, though the loss is still considerable.
3. When peeled and soaked in cold water before cooking, the loss may reach one-fourth of the protein matter.

Similar losses may occur in the cooking of carrots and cabbage.

Breadmaking.—Snyder and Voorhees (40) investigated the losses of flour in breadmaking. They affect both the nitrogen and carbohydrate. The loss in nitrogen may reach 1.45 per cent. The carbohydrate loss is caused by the fermentation which the bread undergoes in "rising" (yeast cells). The authors state that the losses in breadmaking need not exceed 2 per cent. of the flour used, and may be reduced to 1.1 per cent.

Cereal Breakfast-Foods.—The importance of cereal breakfast-foods has been shown especially by the investigations of Woods and Snyder (50). These authors found that cereals comprise 22 per cent. of the total food of a large number of families in this country, furnishing 31 per cent. of the protein, 7 per cent. of the fat, and 55 per cent. of the total carbohydrates. They have separated the large number of cereal breakfast-foods which are on the market into three groups:

1. Those prepared simply by grinding the grain.
2. Those which have been steamed, or otherwise partially cooked, and then ground or rolled.
3. Those which have been acted upon by malt which induces chemical changes in the starch.

The Cooking of Cereals.—The proper cooking of cereals is of more importance than the relative proportions of nutriment they contain. While

definite statements cannot be made regarding the length of time which different cereals should be boiled, all of them require prolonged cooking. They are much more likely to be under- than over-cooked. In general, the more abundant and the tougher the fiber the longer should the process of cooking be continued. For example, whole grains require more cooking than crushed grains. Rice contains but little fiber and may be thoroughly cooked in a relatively short time.

According to Woods and Snyder, it is difficult to know in the case of partially cooked breakfast-foods how much of the necessary cooking has been done in the factory. They point out that over-cooking is harmless, and suggest that further cooking in the home is usually desirable.

Examinations of malted breakfast cereals carried out at the Iowa Experiment Station showed that the largest amount of soluble carbohydrate present was 13 per cent. of the total carbohydrates, the lowest, 0.35 per cent. The average was around 5 per cent. At the Michigan Station it was found that the largest proportion of the soluble carbohydrates in these preparations consists of dextrin. Woods and Snyder state that "the claims made for some brands that the carbohydrates are completely or largely predigested are quite unwarranted."

DIGESTIBILITY OF FOODS[1]

General Considerations.—The term "digestibility" may be understood to mean either the ease and rapidity with which a food is digested, or the completeness of its digestion. This distinction is not always made, however, and confusion has often arisen in the interpretation of the results obtained by different observers. Likewise, when the opinions of physicians and physiologists are not in agreement, the fact is often overlooked that the conditions under which the observations are made are different. Physicians deal with those who are ill, physiologists with those who are well. The term "digestibility" is probably understood by most physicians to mean ease of digestion, by most physiologists completeness of digestion. If these different points of view are borne in mind, discordant opinions may frequently be reconciled.

Foods leave the stomach in the order in which they are digested and liquefied. The length of time they remain in the stomach has been taken by some authors as the measure of their digestibility. While the length of its sojourn in the stomach may not affect the thoroughness with which a food is ultimately digested, it may have an important influence upon subsequent feedings, especially if these be given at short intervals. Delay in gastric digestion often produces in healthy persons unusual or

[1] In the preparation of this section the author has derived much information from U. S. Dept. of Agriculture Bull. No. 85, and Farmers' Bulls. Nos. 85, 121, 128, 182.

uncomfortable sensations referable to the stomach. In persons who are ill, delay of gastric digestion may not only interfere with the frequency of the feedings, but may cause loss of appetite, nausea, and even the rejection of food.

The nutritive values of foods cannot always be measured by the amounts of the different foodstuffs they contain. They depend rather upon the extent to which these foodstuffs may be digested and absorbed. While it is generally believed that the greater part of most foods is digested and absorbed by healthy men, our knowledge of the extent to which they are utilized by persons who are ill is far from complete.

A number of factors affect the digestion and utilization of foods. Some of the more important of them may be considered.

The favorable influence of appetite upon digestion has been known so long that it is best expressed in the form of the adage, "Hunger is the best sauce." It was only about twenty years ago, however, that Pavlov established the popular belief upon a scientific basis through his discovery that the desire for food induces a reflex stimulation of gastric juice. Pavlov calls this secretion the "appetite" or "igniting juice." Its function is to initiate the digestive process, which then proceeds more or less automatically through the stimulating action of the products of digestion upon the gastric glands. Food eaten without appetite may lie in the stomach unchanged for hours. Physicians have made use of this knowledge for many years, and have striven to arouse an appetite in patients when it was lacking. Another, and related, adage, "Laugh and grow fat," finds application here. Meals eaten amid cheerful surroundings and in pleasant company are taken with greater zest and enjoyment, and are more easily digested.

The ease and completeness of digestion also depend in general upon the amount of food which is eaten at a time; the greater the quantity the less rapidly, and probably less thoroughly, is it digested. Overeating is a common cause of digestive disorders. The custom of taking three meals a day is based upon the general experience of mankind that the amount of food required can be handled with less tax upon the digestive organs when distributed in this manner.

Careful regulation of the quantity of food allowed at one time is of even more importance when persons are ill or have "weak" digestions. The common practice of giving small quantities of food at frequent intervals to persons with enfeebled powers of digestion is supported by the experiments of Pavlov, who found that if food was given to a dog in small quantities at intervals, the gastric juice was stronger than if the whole ration had been given at once. Moreover, the appetite of an invalid is often impaired by even the sight of large "portions" of food.

Experiments upon healthy men have repeatedly shown that a well-balanced dietary is digested more thoroughly than a single food. The

significance of such observations, with respect to the arrangement of dietaries for invalids, is apparent.

The secretion of gastric juice is intimately related to the quantity of water in the body (Pavlov). Water is drawn from the blood by the cells of the gastric glands as they elaborate the secretion. If the supply of water is not sufficient, the digestive juices are deficient in quantity, and digestion is impaired. Therefore, water should be supplied to the body by enemata or otherwise, as an aid to digestion, in diseases attended by its loss in large quantities, such as excessive vomiting, profuse diarrhea, and hemorrhages. "Every food determines a certain amount of digestive work, and when a given dietary is long-continued, definite, and fixed, types of gland activity are set up which can be altered but slowly and with difficulty. In consequence, digestive disturbances are often instituted, if a change be made suddenly from one dietary régime to another, especially from a sparse to a rich diet." (Pavlov). It should be added that patients cannot all be fed alike, even when suffering from the same disease. Prejudices and idiosyncrasies to foods are not removed by illness, and must be recognized. Variety in food is sought in health and should be permitted in disease to the extent which is compatible with the patient's well-being.

Digestibility of Meats.—Numerous observations concerning the digestibility of meats have been made upon healthy men. Valuable data have also been obtained by Pavlov and his co-workers from their experiments upon dogs. But we possess very little information respecting the digestibility of meats in various diseases. The conclusions drawn from experiments upon healthy men refer particularly to the thoroughness of digestion. They should not be applied without caution to persons who are ill, and who, on that account, may digest meat slowly and with difficulty.

Probably the most important conditions affecting both the rate and completeness of digestion of meat are the amount of connective tissue and fat it contains, and the method and duration of the cooking.

The "appetite" juice plays a less important rôle in the digestion of meat than in the digestion of eggs and bread. This is due to the presence of extractives in meat, which are direct excitants of the gastric glands. According to Pavlov, the secretion of "meat juice" is the most rapid of all. Raw meat, introduced unnoticed into the stomach of a dog, excites secretion within 15—30 minutes. But if meat be freed from extractives by prolonged boiling, and the water be forced from it by compression, it has no stimulating effect upon the gastric glands.

The influence of the connective tissue upon the digestion of meat is mainly mechanical, though the mastication of tough, fibrous meat is not attended with pleasure. The presence of much connective tissue prevents free access of the digestive juices to the muscle fiber, and affects both

the rapidity and completeness of digestion. The practice of pounding meat across the cut ends has for its object the separation of the muscle fibers from the connective tissue. Likewise, the prolonged cooking of meat converts the connective tissue into gelatin, and frees the muscle fibers, though they are probably rendered slightly less digestible by the process.

The Influence of Fat-Content Upon the Digestion of Meat.—Meats vary in the amount of fat they contain. Dried meat may not have more than 3 per cent of fat, while pork may contain as much as 50 per cent. The presence of fat inhibits the secretion of gastric juice, and prolongs the stay of both protein and carbohydrate in the stomach. Therefore, the rapidity of the digestion of meat bears a direct relation to the amount of fat it contains. Fat meats, such as pork, are well known to be difficult of digestion.

While but little attention has been devoted to the percentages of the different meats which are absorbed, it is probable that meat of all kinds, whether raw or cooked, is very completely absorbed by healthy men—nearly all of the protein and about 95 per cent. of the fat.

Our knowledge of the digestibility of meat in disease is confined largely to the results of clinical observation. While carefully made observations of this kind have a definite value, it is desirable that they should be confirmed by experiment. Yet, one of the conspicuous features of Pavlov's work is the frequency with which he has confirmed both popular and clinical beliefs respecting digestion.

In giving meat to invalids, every precaution should be taken which will make for rapidity of digestion. It should be served attractively and in not too large "portions" in order to promote the secretion of the "appetite" juice. If given raw, it should be finely scraped, as this separates the fibers from the connective tissue. Raw meat should not be forced upon a patient, since it is not certain that raw meat is more quickly digested than slightly cooked meat. If cooked too long, the muscle fibers become hard, tasteless to many persons, and difficult to digest. Furthermore, meats which contain relatively little fat should be selected for invalids.

Poultry is popularly supposed to be more easily digested than red meats. As no experiments contradict this belief, it may provisionally be accepted. If true, it is probably due to the tenderness of the fiber and the relatively small proportion of fat. The fatter kinds of poultry are less easily digested than the lean. The popular belief that the light meat is more digestible than the dark may be due to the higher proportion of fat in the dark meat, but the difference is slight.

Attention should be directed here to the fact that the extractive-content is essentially the same in white and red meats. In diseases where it is desirable to reduce the purin bodies to a minimum there is no advan-

tage in prohibiting red meats, if the patient is allowed to eat poultry at will. It is probably true, so far as the sick are concerned, that the only difference between white and red meats concerns ease of digestion.

Digestibility of Fish.—The relative digestibility of different fish appears to be dependent upon the amount of fat they contain. Langworthy (26) has grouped the commoner fish, from this standpoint, into three classes:

1. Fish containing over 5 per cent. of fat: Salmon, shad, herring, Spanish mackerel, and butterfish.

2. Fish containing between 2 per cent. and 5 per cent. of fat: White-fish, mackerel, mullet, halibut, and porgy.

3. Fish containing less than 2 per cent. of fat: Smelt, black bass, bluefish, white perch, weakfish, brook-trout, hake, flounder, yellow perch, pike, pickerel, sea bass, cod, haddock.

Digestibility of Eggs.—Most of the experiments upon the digestibility of eggs have been made upon healthy men and lower animals. All of them indicate that eggs are easily and thoroughly digested. Rubner found that with a diet consisting of hard-boiled eggs alone the nitrogen was absorbed to about the same extent as that of meat, while the fat was absorbed better than the fat of meat. Aufrecht and Simon (3) studied the absorption of lightly boiled and raw eggs, compared with meat, as part of a mixed diet, and found that the absorption of both the nitrogen and fat was greater in the egg—than in the meat—period. They concluded that lightly boiled and raw eggs have a higher food value as part of a mixed diet than a corresponding amount of meat.

The method of cooking eggs appears to affect the rate rather than the completeness of their digestion. While this has no appreciable effect in health, it may cause disorders of digestion in disease. Judged by the length of time they remain in the stomach, eggs are digested in the following order (the most easily digested are given first):—lightly cooked eggs, raw eggs, buttered eggs, hard-boiled eggs, omelette. Judged by the completeness of absorption, Aufrecht and Simon have shown that lightly boiled eggs have a somewhat lower nutritive value than raw eggs. Jorissenne believes that if hard-boiled eggs are thoroughly masticated they are digested as easily as lightly cooked eggs. Very few experiments have been made upon the relative digestibility of the white and the yolk of the egg. Stern found that raw or half-raw yolk is readily digested.

While it is probable that the facts regarding the digestibility of eggs by healthy men apply equally to those who are ill, positive statements to this effect cannot be made. Probably the most important factor influencing the digestibility of eggs in disease is whether they are taken with relish. White of egg eaten without appetite will lie in the stomach unchanged for a considerable time (Pavlov). This is due to the fact that the egg contains no substances like the extractives of meat which are

capable of exciting the flow of gastric juice. Once the flow is started, the products of digestion stimulate further secretion. If water be taken with egg-albumin it initiates the secretion (Pavlov). A similar result is obtained if the egg is preceded by, or given with, meat broth. The difference in digestibility between lightly cooked and raw eggs is so slight that it is not necessary to compel patients to take them raw. When a patient's digestive powers are much enfeebled, eggs should not be buttered, but there is no objection to the addition of salt and pepper. Fraser found in experiments upon the artificial digestion of eggs that tea, coffee, and cocoa retarded digestion of the protein, though the effect of coffee was less marked than that of the others.

Idiosyncrasy to Eggs.—Persons are seen occasionally who have an idiosyncrasy against eggs. The peculiarity is usually discovered early in life. The symptoms develop after eating egg even in small quantities and irrespective of whether it is taken alone or combined with other foods, as in custards. The symptoms are often severe; collapse may occur. Urticaria is common.

The Digestibility of Milk.—The following account of the digestibility of milk is taken principally from Pavlov. There are three properties of milk which secure it an exceptional position. Milk, when compared with other foods in nitrogen equivalents, requires the weakest gastric juice and the smallest quantity of pancreatic fluid. Consequently, the secretory activity necessary for its assimilation is much less than for any other food. When milk is introduced mechanically into the stomach of an animal, it causes a secretion both from the stomach glands and also from the pancreas, consequently it appears to be an independent chemical excitant of the digestive canal, and in this action there is no essential difference whether the milk be introduced directly into the stomach or be given the animal to lap. Milk excites not only a really effective, but also a very economic secretion, and the appetite is unable to stimulate this secretion into a more active or abundant flow. The price which the organism pays in digestive work for the nitrogen of milk is much less than for other foods.

Idiosyncrasy to Milk.—In rare instances persons exhibit an idiosyncrasy against milk. Halberstadt (17) considers this to be evidence of a congenital constitutional anomaly. The idiosyncrasy may be against the albumin, fat, or whey. In some cases the deleterious effects of milk are thought to be due to a change it causes in the flora of the intestine. Definite poisoning occurs in these cases, often accompanied by inflammatory changes in the alimentary tract, and must be differentiated from the digestive disturbances, which, many physicians claim, are always caused by milk. Tugendreich (43) has described a similar poisoning under the title of "Buttermilk Fever."

Digestibility of the Carbohydrates.—The digestibility of the carbohydrates depends in general upon the relative proportions of starch (or

sugar) and cellulose. The greater the amount of cellulose and the thicker the cell walls the less digestible is the food. The preparation of certain foods, such as the milling of grain, has for its object the removal of the greater portion of the cellulose. Sugars may be regarded as partially digested carbohydrates. Except when taken in quantities, and in mixtures, which interfere with the normal processes, they are easily digested and completely absorbed. Carbohydrates leave the stomach quickly.

Bread and cereals may be taken as types of the carbohydrate foods.

Digestibility of Bread.—Bread is generally considered to be an easily digested food, but the "appetite" juice is necessary for its perfect digestion. Bread eaten without appetite may lie in the stomach for a long time without change. Bread is digested chiefly by the pancreatic secretion. The lactic acid which is formed in the stomach stimulates the pancreas and thus aids the digestion.

The majority of the experiments on the digestibility of bread relate to the completeness of its digestion by healthy men. Myer and Voit, experimenting with different kinds of wheat and rye bread, found that the digestibility of bread depended chiefly upon its lightness. Studies carried out at the Minnesota Experiment Station upon the digestibility of breads made from graham, whole wheat, and standard patent flours demonstrated that bread made from standard patent flour was most completely digested, whole wheat bread next, and graham least. The digestibility of crackers, macaroni, and various sweet cakes, made from white flour was found at the same Station to be essentially the same as that of bread.

There is a popular belief that cold bread is more easily digested than hot bread. This is probably true but it is due to the physical condition of the bread and not to the heat. Hot bread is moist, and, if not soggy before being eaten, is compressed into tough masses during mastication, and thereby rendered less *easily* digestible. If properly made, cold or stale bread contains less moisture and is not open to the same objection.

As far as is known the above facts are applicable in disease. Du Bois found that bread and crackers are easily and completely digested by typhoid fever patients.

When bread and similar foods are eaten by persons who have little or no appetite, they should be combined with substances which have a local stimulating action upon the gastric glands. Water is sufficient for the purpose, but meat broth is often to be preferred.

Digestibility of Cereal Breakfast Foods.—The digestibility of cereal breakfast foods has been investigated at the Connecticut, Maine, and Minnesota Experiment Stations. The results showed that in healthy men the cereal breakfast foods in general are somewhat less digestible than white bread. It was found at the Michigan Experiment Station that the greater

part of the soluble carbohydrates in the so-called predigested breakfast foods consists of dextrin.

Digestibility of Fat.—Fat illustrates especially well the distinction which must be made between ease and completeness of digestion. All healthy persons consume daily larger or smaller quantities of fat in the form of butter, cream, or the native fats contained in other foods. But an excess of fat over the usual quantity or a change in its form is distasteful to many persons, difficult to digest (as regards the stomach digestion), and may produce nausea. Nevertheless, if it is tolerated by the stomach, only a small portion of the fat ingested escapes absorption in health.

Fat is not digested in the stomach, but may have an important influence on gastric digestion. Fat exerts an inhibitory action upon both the psychic or "appetite" and local gastric juices, and delays the passage of the chyme into the duodenum (Pavlov). The inhibitory action of fat affects especially the digestion of protein, and explains the well-known fact that fatty protein foods are difficult to digest, whether the fat be native to the food or be added to it in the process of cooking. On the other hand, the addition of fat to starchy foods, for example, bread and butter, is customary, and, according to Pavlov, rational. Bread requires little gastric juice for its digestion; the fat restrains the activity of the gastric glands, while at the same time it promotes the secretion of pancreatic juice, which is needed for the digestion of the starch, the partially digested protein, and the fat itself. Though an excess of fat in a mixed meal may cause disturbances of digestion, fat alone, even when taken in relatively large quantities, is not difficult to digest.

Large amounts of fat may cause regurgitation of the duodenal contents into the stomach. This fact has been observed both experimentally and clinically (Bassler, 5).

Ordinarily, fat is well absorbed in health. Its absorption appears to be related in a measure to its melting-point. Butter, with a melting point of 37° C., is more completely absorbed than mutton-fat, with a melting-point of 52° C. When the food contains 80-100 grams of fat, only 4-6 per cent. is lost normally in the feces.

The absorption of fat varies greatly, however, in disease. According to Umber (44), 45 per cent. of ingested fat may be lost in the feces when the bile duct is occluded. In disease of the pancreas the loss may reach 75 per cent. On the other hand, the absorption of fat in typhoid fever is often remarkable. Some of my patients, studied by Du Bois, when taking 250 grams of fat a day in the form of cream and butter, lost an average of 7.2 per cent. in the feces; in the steep-curve period and in convalescence, while taking similar amounts, they lost 4.5 per cent.

Length of Time Food Remains in Stomach.—The length of time which a food remains in the stomach has often been accepted as the meas-

ure of its digestibility, but is probably only an indication of the ease of its digestion.

The length of time which certain foods remain in the stomach is shown in the following table of experiments by Penzoldt (34):

Grams	
	1—2 HOURS
100–200	Water.
220	"Charged" water.
200	Tea (Without admixture.)
200	Coffee (Without admixture.)
200	Cocoa (Without admixture.)
200	Beer.
200	Light wine.
100–200	Boiled milk.
200	Meat broth.
200	Peptone in water.
100	Soft-boiled egg.
	2—3 HOURS
200	Coffee with cream.
200	Cocoa with milk.
200	Malaga wine.
300–500	Water.
300–500	Beer.
300–500	Boiled milk.
100	Raw, scrambled, hard-boiled egg and omelette.
250	Calf's brain, boiled.
12	Raw oysters.
200	Boiled carp.
200	Boiled pike.
200	Boiled haddock.
200	Dried codfish.
150	Boiled cauliflower.
150	Cauliflower salad.
150	Boiled asparagus.
150	Potato.
150	Potato soup.
150	Cherry preserves.
150	Raw cherries.
70	White bread, fresh or old, dry or with tea.
70	Cracknel.
50	Albert biscuits.

3—4 HOURS

Grams	
230	Boiled young fowl.
230	Roast partridge.
220–260	Boiled pigeon.
195	Roast partridge.
250	Beef, raw or cooked.
250	Boiled calf's foot.
160	Ham, raw or cooked.
100	Roast veal, warm or cold.
100	Broiled beeksteak, cold or warm.
100	Scraped raw beefsteak.
100	Tenderloin.
200	Rheinsalmon, boiled.
72	Caviar.
150	Rye bread.
150	Graham bread.
100–150	Albert biscuit.
150	Boiled rice.
150	Boiled cabbage.
150	Boiled carrot.
150	Spinach.
150	Raw radish.
150	Apple.

4—5 HOURS

210	Roast pigeon.
250	Broiled filet of beef.
250	Broiled steak.
250	Smoked tongue.
100	Smoked meat.
250	Roast hare.
240	Roast partridge.
250	Roast goose.
250	Roast duck.
200	Salt herring.
150	Lentil soup.
200	Pea soup.

Coefficients of Digestibility (Absorbability) in Different Groups of Food Materials[1]

Kind of Food	Protein	Fat	Carbohydrates
	%	%	%
Meats and fish	97.0	95.0	....
Eggs	97.0	95.0	....
Dairy products	97.0	95.0	98.0
Animal food (of mixed diet)	97.0	95.0	98.0
Cereals	85.0	90.0	98.0
Legumes (dried)	78.0	90.0	97.0
Sugars	....	....	98.0
Starches	....	....	98.0
Vegetables	83.0	90.0	95.0
Fruits	85.0	90.0	90.0
Vegetable foods (of mixed diet)	84.0	90.0	97.0
Total food (of mixed diet)	92.0	95.0	97.0

THE EFFECTS OF STARVATION

It will be necessary to distinguish between the effects of complete and of partial deprivation of food. Starvation is complete when a person receives no food and the energy necessary for the continuance of life is derived from his own body. Partial starvation occurs when a person receives only a portion of the food he requires. Under such circumstances the tissues of the body are drawn upon for only part of the necessary energy. In actual practice, however, the physician must take into consideration the possible disturbances of metabolism produced by the disease from which the patient is suffering, and which also may be a cause of the starvation.

The Effects of Complete Starvation.—Complete abstinence from food for short periods is not—or, at least, is not likely to be—harmful in the case of adults. Nature provides for such emergencies by accumulating reserves of glycogen and fat. Young children, on the other hand, do not bear starvation well, even for short periods. The reserve supply of glycogen is relatively small, and is soon exhausted. After its exhaustion, the body derives all of its energy from protein and fat. Fat, which is of lesser importance, is sacrificed in favor of protein. The heavy demand made upon the fat results in its incomplete combustion and the occurrence of acidosis with acetone bodies in the blood and urine.

The expenditure of energy by the body remains normal for the first day or two of complete starvation. Rubner reckons it at 30—32 calories per kilogram of body weight. When the subject is at *absolute rest*, however, the heat production may fall to 22—26 calories per kilogram (Atwater, Tigerstedt, Magnus-Levy). These figures represent the minimal

[1] From U. S. Dept. of Agriculture Farmers' Bulletin No. 142.

metabolism compatible with life, and cannot be applied in practice, because patients are rarely or never at complete rest, unless they are asleep or in coma.

Loss of weight is characteristic of starvation. It is due to the consumption of the body tissues and to the elimination of water and salts. As the weight diminishes, the expenditure of energy falls, the fall, according to Rubner (35), corresponding to the loss in weight. The body temperature remains practically constant. The urine is diminished in amount. The loss of nitrogen is large for the first day or so, after which it remains fairly constant (10—13 grams) for a week or ten days. Material divergence from these figures indicates the influence of disease.

Benedict (6) has shown that recovery from starvation is rapid in health and may be followed by an actual gain in weight. Fasting for short periods appears to stimulate the body to increase its store of fat. This is regarded by Benedict to be a protective mechanism.

The Effects of Partial Starvation.—Partial starvation may occur through force of circumstances, such as poverty, or as the result of disease. In the latter case it is not always easy to distinguish between the influence of insufficient food and that of the disease. From the medical standpoint partial starvation probably occurs with greatest frequency in prolonged febrile and in malignant diseases.

The body is capable of regulating its expenditure of energy to some extent. When the food supply is insufficient the production of energy falls correspondingly. But Von Noorden (45) believes that the minimal amount of energy required by persons who are bedridden, or who remain indoors and do but little work amounts to 30—32 calories per kilogram. Their diets should be arranged upon this basis. Persons who are underfed economize their protein at the expense of the less important fat. The longer the deprivation of food continues the smaller the relative amount of protein consumed.

It should be added that persons who are undernourished are less able to resist invasion by bacteria and to combat infection.

THE EFFECTS OF OVERFEEDING

A person is overfed when he takes and absorbs more food than is required for his energy exchanges. If an excess of food is not digested and absorbed, it is likely to cause alimentary disturbances.

The effects of overfeeding may be either physiological or pathological, that is, the general condition of the person may be improved, or various disturbances of function may be brought about. We are concerned here chiefly with the physiological effects of overfeeding.

A person who is overfed gains in weight, largely through the deposi-

tion of fat, though there may be a coincident retention of nitrogen. Fat is a relatively inactive tissue from the metabolic standpoint. The accumulation of fat adds to the reserves, but does not increase the power of the body. Improvement in tone, if not growth, of muscle is necessary to bring the body into a state of vigorous health. This depends to a great extent upon proper exercise, and should be borne in mind when one is employing the overfeeding cure.

The objects to be sought in overfeeding may be either the accumulation of fat, or improvement in the condition of the muscles, or both. In arranging the diet the effects of the different foodstuffs must be taken into consideration. Fat is the best food for simple fattening purposes, because foreign fats are deposited in the body without change and with the expenditure of very little energy. Carbohydrate ranks next to fat in value. It has been estimated that one-fourth of the potential energy of carbohydrate is lost before it is deposited as fat. Protein is least valuable because of the increase it causes in metabolism and because it cannot add materially to the store of fat. Therefore, an increase in protein alone is irrational in overfeeding cures. Von Noorden (46) advises specifically against the employment of proprietary protein foods for such purposes. Even in convalescence from infective diseases an increase of protein does not materially affect the retention of nitrogen.

While the experiments of both Krug (21) and Dapper (14) indicate that an increase in the carbohydrate ration and a relatively greater increase of fat are accompanied by a retention of nitrogen in lower animals, this fact has not yet been established for man except in typhoid fever. Typhoid fever patients may retain nitrogen during the course of the disease and in convalescence when the diet furnishes an excess of both carbohydrate and fat (Shaffer and Coleman, 38).

General clinical experience appears to indicate that the most suitable diet for an overfeeding cure is rich in both fat and carbohydrate. The Voit or Atwater standard should be followed in determining the amount of protein. In all cases the total energy requirement of the patient should be calculated and the diet arranged to furnish more energy than the calculation calls for.

While the pathological effects of overfeeding cannot be considered at length, attention should be called to the fact that injudicious overfeeding may cause pathological obesity.

METHODS OF ARTIFICIAL FEEDING

When for any reason patients cannot or will not take food by mouth, other methods of nourishing them must be employed.

Rectal Feeding.—Rectal feeding may be resorted to when swallow-

ing is difficult or impossible as in cases of tumor or stricture of the throat or esophagus; when the muscles of deglutition are paralyzed; in cases of ulcer or tumor of the stomach; and in cases of uncontrollable vomiting. When for any reason patients are incapable of taking all of the food they require by mouth, additional food may be given for brief periods per rectum.

The nutritive value of nutrient enemata has, according to recent investigations, been greatly overestimated, and the physician should keep clearly in mind the fact, when employing this method of alimentation, that the patient is receiving only a portion of the food he requires. Patients have subsisted upon nutrient enemata for several weeks, but it has been largely at the expense of the body tissues. The gains in weight which have occurred, especially after severe hemorrhages, have been shown to be due to retention of water. Probably the greatest quantity of food which a patient is capable of absorbing by rectum reaches only 1/4—1/3 of the total daily requirement, even when at rest in bed. Boyd (7) calls attention particularly to the fact that the amount of food absorbed depends upon the patient's capacity for absorption, and not upon the quantity of food injected. Therefore, it is not always desirable to give large enemata: the unused portion is likely to decompose and cause irritation.

Nutrient enemata do not enter the ileum, and such absorption as occurs must be from the colon. Nor do nutrient enemata cause a reflex secretion of gastric juice (Pavlov).

The different foodstuffs are not absorbed with equal facility by the colon. All of the available evidence indicates that protein is poorly absorbed. Brown (8) compared the nitrogen output in the urine from saline and nutrient enemata, and observed not only that the curves were similar, but that they were comparable to the nitrogen excretion of healthy fasting men. When the same amount of food was given by mouth the nitrogen of the urine rose at once. Therefore, since but little protein is absorbed, and since proteins are readily decomposed by the intestinal flora, giving rise to substances which may irritate the bowel, it appears to be undesirable to give nutrient enemata containing protein even in its partially digested forms.

There is a difference of opinion regarding the absorption of fat. Brown was unable to prove the absorption of emulsified and pancreatized fats when given by rectum to a patient suffering from chyluria, though when fat was taken by mouth the amount in the urine was promptly increased. Boyd, on the other hand, has shown that fat may be absorbed, though he calls attention to the wide differences in the absorptive power of different individuals. Boyd recommends yolk of egg and emulsified olive oil as suitable fats for nutrient enemata. Cream has also been used.

Dextrose is readily absorbed by the large intestine, and is probably the best form in which to give carbohydrate. Dextrin has also been

recommended. Brugsch (9) states that dextrinized or malted starch is less irritating than the sugars, and may be employed instead of them. Brown was able to raise the respiratory quotient by the use of dextrose and to cause the diminution or disappearance of acidosis. Dextrose may irritate the bowel and cause cramp-like pains when given in concentration greater than 10 per cent. I have found it necessary at times to reduce the strength of the solution to 7 per cent. and even to 5 per cent. If sugar is absorbed by the inferior hemorrhoidal veins, it enters the general circulation without passing through the liver, and may cause glycosuria.

Salts and water are readily absorbed by the colon, and there is little doubt that much of the benefit which has been ascribed to nutrient enemata was attributable to these substances. Alcohol, likewise, is readily absorbed, and is often added in small quantities to enemata.

Formulæ for Nutrient Enemata.—		Calories.
Dextrose,	20–30 grams	80–120
Water,	200–300 c. c.	
Dextrose,	20–30 grams	80–120
Wine (white or red),	15–30 c. c.	10–20
Water,	200–300 c. c.	
Boas recommends:		
Milk,	250 c. c.	175
Yolk of egg,	2	100
Salt,	A pinch.	
Wine,	15 c. c.	10
Flour,	15 grams	56
Myer recommends:		
Cream,	250 c. c.	500
Peptone,	25 grams	?
Pancreatin,	5 grams	

Method of Giving Nutrient Enemata.—A cleansing enema of normal salt solution (0.9 per cent.) should be given every morning one hour before the nutrient enema. Some authors recommend a cleansing enema before each nutrient enema, but unless the nutrient enema contains foods which are not readily absorbed this procedure scarcely seems necessary, and may increase the irritability of the colon. The patient should be placed either upon the left side or the back with the hips elevated on a pillow. The ap-

paratus may consist of a medium-size funnel inserted into the end of a small rectal tube or large catheter, or an inverted thermos bottle connected with the rectal tube or catheter by means of rubber tubing. A small metal tube passed through the stopper and reaching to the bottom of the bottle permits the entrance of air and the flow of its contents. A bulb-syringe is not suitable because of the difficulty of controlling the pressure, and the likelihood of injecting air. The funnel-apparatus is perhaps more convenient for thicker enemata; the bottle, for the sugar solutions. The rectal tube should be oiled, freed of air by allowing the enema to fill it, and introduced well into the intestine.

The size of nutrient enemata varies from six to ten ounces (200-300 c. c.); the larger the enema the less frequent the need of repetition. They should be given at temperatures of 95° to 100° F. Nutrient enemata should always be injected slowly. The flow may be regulated by raising or lowering the container. The sugar solutions are often given drop by drop, after the Murphy method. It is rarely advisable to give more than three enemata a day.

The patient should be instructed to remain quiet afterward and to resist expulsion of the enema. Pressure upon the perineum with a folded towel by the attendant will often enable a patient to retain it when otherwise it would be rejected. When the colon becomes irritated, 10 to 20 drops of laudanum may be added to the enema.

Gavage.—The term "gavage" designates forced feeding through an esophageal tube. The tube may be passed through the mouth or the nose. Gavage is especially indicated in the case of hysterical or psychopathic patients who refuse food. It has also been employed in stricture of the esophagus, whether spasmodic or organic, in paralysis of the muscles of deglutition, and in comas. The practice of gavage is not unattended by danger, since the tube may enter the larynx, especially when the patient is unconscious, and cause pneumonia. Food should not be administered in such cases oftener than once or twice a day. In the case of persons who are conscious, food may be given three times a day.

Only liquid foods are suitable for gavage. The "meal" should be made up (as to bulk and energy value) according to the frequency with which it is to be repeated, and should be warmed to about the body temperature. Milk, cream, eggs, and sugars are best adapted to the method, and may be employed in the following or similar mixtures:

		Calories.
Milk	1 pint (500 c. c.)	350
Cream	1 pint (500 c. c.)	1,000
Lactose or cane-sugar..	50 grams	200
		1,550

		Calories.
Milk	1 pint (500 c. c.)	350
Cream	½ pint (250 c. c.)	500
Eggs	2	160
		1,010

Subcutaneous Feeding.—*Fats.*—Leube (24) first suggested the subcutaneous administration of oils and fats as a means of supplying the body with nutriment. Mills (31) has recently made an extended study of the method in Lusk's laboratory, and the following statements are based upon his results.

Fats which are similar in composition to that of the body are most readily absorbed. Emulsions are absorbed better than plain oils. The best emulsion is made with 3—5 per cent. of egg-lecithin and sterile water. The site of the injection should be sterilized with tincture of iodin and should be massaged gently afterward. Care should be taken to avoid entering a vein, as cerebral or pulmonary fat embolism would result. If the emulsion is injected slowly into the subcutaneous tissues, 60 grams of oil may be given at one time without causing discomfort. Mills has proved that fats introduced subcutaneously may be burned directly, thus sparing the body fat, may be retained in the body in their own form, or may be reconstructed into body fat.

The subcutaneous administration of fat should not be employed unless the patient is capable of taking food by mouth. While the method holds promise of being useful, it has not been perfected sufficiently to permit of its recommendation for general purposes.

Protein and Sugar.—While numerous attempts have been made to administer proteins and sugar subcutaneously, the methods hitherto employed have not proved practical. Native protein solutions are difficult to sterilize: proteoses and peptones are toxic. Solutions of glucose cause pain, and may cause necrosis, when given in greater concentration than 5 per cent. The weaker solutions supply so little nourishment that the drawbacks to the method outweigh its advantages.

THE SALT-POOR DIET

The diet of civilized man contains ordinarily from 10 to 15 grams of common salt. This amount is readily excreted by normal kidneys in 24 hours. In some cases of nephritis, however, especially those of the parenchymatous type, the kidneys are unable to excrete more than 2 or 3 grams, or even less, of salt a day. The salt which is retained passes into the tissue fluids and causes, or increases an existing, edema. The in-

ability of the kidneys to excrete salt sometimes runs parallel with an inability to excrete water.

The excretory power of the kidneys for salt may be tested by a diet of 3 liters of milk (this contains 5 grams sodium chlorid and 100 grams protein) or by Strauss' (42) diet, consisting of 3/4 liter of milk, 4 eggs, 150 grams of bread, and enough fruit, fruit juice, tea, and sugar to make it palatable. Strauss' diet contains about 3 grams of salt. If the kidneys are able to excrete the amount of salt contained in these diets, salt may be added to either of them in quantities of 5 to 10 grams. When the kidneys are unable to eliminate the normal quantity of salt, some form of salt-poor diet may be advised, but it should be stated that the salt-poor diet has not entirely fulfilled the promises held out for it.

A salt-free diet is a practical impossibility unless one follows von Noorden's plan of giving 200 grams of lactose only. The salt-poor diets have been grouped under three headings:

The strict salt-poor diet of Widal (49) (containing 1.5 to 2.5 grams of salt) consists of salt-free bread 200 grams, meat 200 grams, vegetables 250 grams, butter 50 grams, and sugar 40 grams. This diet contains 60 grams of protein, and furnishes 1,500 calories, which is nearly sufficient energy for the average patient resting quietly in bed.

The medium strict diet contains from 2.5 to 5 grams of salt. The milk diet (3 liters) belongs here. The food should be cooked without the addition of salt, but the patient should be allowed to use 2 to 3 grams of salt a day at the table.

The moderate salt-poor diet (5 to 10 grams) allows considerable latitude. It is not necessary to prepare special dishes, but the cook should be instructed to use salt sparingly. Salted foods, such as bacon and ham, should be prohibited. This diet furnishes only a rough control of the salt intake.

In administering a salt-poor diet, it is important that the energy value of the food should not be permitted to fall below, nor to greatly exceed, the daily requirement of the patient.

In addition to its employment in nephritis, the salt-poor diet has been recommended for the edema of chronic cardiac valvular disease, for the ascites of cirrhosis of the liver, pleurisy with effusion, arterial sclerosis, and diabetes insipidus.

SALT CONTENT OF FOODS[1]

According to Leva

	% Sodium Chlorid in Raw Material		% Sodium Chlorid in Raw Material
MEATS		**MEAT EXTRACTS**	
Mutton	0.17	Liebig's	2.60
Veal	0.13	Kemmerich	1.40
Calf's brain	0.20	Various bouillon capsules, extracts, etc	9.40—22.0
Calf's kidney	0.32		
Calf's liver	0.14	**PREPARED FOODS**	
Beef (lean)	0.11	Plasmon	0.21
Pork (lean)	0.10	Roborat	0.0051
FISH		Sanatogen	0.42
Trout	0.12	Somatose	0.66
Halibut	0.30	Bovril's preparations	0.26—14.1
Herring	0.27	Valentine's Meat Juice	0.08—1.20
Cod	0.16	Egg (white and yolk)	0.21
Carp	0.086	Egg (white alone)	0.31
Salmon	0.061	Egg (yolk alone)	0.039
Mackerel	0.28	Caviar	3.00
Haddock	0.39	Milk (whole)	0.16
POULTRY		Cream	0.13
Duck	0.14	Buttermilk	0.16
Goose	0.20	Whey	0.11—0.15
Chicken	0.14	Condensed Milk	0.40
Pigeon	0.15	Butter (unsalted)	0.02—0.21
Turkey	0.17	Butter (salted)	1.00—3.00
Venison	0.11	Peanut butter*	4.10
Oyster (washed)	0.52	Oleomargarine	2.15
Oyster (with sea water)	1.14	Palmin	0.0016
SMOKED AND SALTED FOODS		Fructin	0.10
Ham (raw)	4.15—5.86	**CHEESE**	
Ham (boiled)	1.85—5.35	Parmesan	1.93
Salmon (smoked)	7.50	Swiss	2.00
Bacon (smoked, German)	1.01	American, pale*	0.82
Bacon (smoked, American)	11.61	Pineapple cheese	2.13
Corned beef, German	2.04	Edam	3.30
Corned beef, American	11.52	English cream cheese	0.70—1.15
Cod (salt)*	23.00	**INFANT'S FOODS**	
Cod (salt, boneless)*	19.00	Nestlé's Food	0.29
Herring (smoked)*	11.70	Rademan's	0.03
Mackerel (salt, dressed)	10.40	Robinson's Patent Groats	Trace
Salmon (smoked, salted)	10.87	**BREAD, ETC.**	
Sardines (French, in oil)	1.34	Graham bread	0.61
Cod-liver oil	0.17	Pumpernickel	0.46
Gelatin (dry)	0.75	White bread	0.18—0.70
Beef marrow	0.11	Zwieback	0.38
Sausages, Frankfurter	2.20	Macaroni	0.067
Sausages, various kinds	2.90—8.10		
Anchovy paste (Cross & Blackwell)	40.1		

[1] Analyses marked thus * from Atwater and Bryant (2).

SALT CONTENT OF FOODS—*Continued*

	% Sodium Chlorid in Raw Material
CEREALS, ETC.	
Barley	0.037
Oats	0.046
Rye	0.014
Wheat	0.013
Rice	0.039
Corn (maize)	0.019
Wheat flour	0.002—0.008
Oatmeal (American)	0.29
Oatmeal (German)	0.28
Quaker Oats	0.082
Sago	0.19
VEGETABLES	
Potatoes	0.016—0.078
Beets	0.058
Beans	0.09
Peas	0.058
Lentils	0.13—0.19
Lentils (dried)	0.155
Artichokes	0.036
Cauliflower	0.05—0.15
Cucumber (fresh)	0.06—0.08
Horse-radish	0.02—0.06
Radish	0.075
Celery, stalks	0.25—0.49
Celery, roots	0.089
Asparagus	0.04—0.06
Spinach	0.084—0.21
Tomatoes	0.094
Cabbage	0.11—0.44
Onions	0.016—0.09
CANNED VEGETABLES	
Green corn*	0.40
Green peas*	0.70
Tomatoes*	0.10
Mushrooms	0.04—0.06
FRUITS	
Pineapple	0.071
Orange	0.0057—0.0550
Apricot	0.0047
Lemon	0.0045
Strawberry	0.0100—0.020
Chestnuts	0.0045—0.010
Cherry	0.013
Cocoanut juice	0.035
Olives	0.008—0.210
Plum	0.0046
Gooseberry	0.021
Watermelon juice	0.011
FRUITS—*Continued*	
Grape	0.024
Almonds, dry	0.010
Walnuts, dry	0.019
Cane sugar	0.110
Lump sugar	0.049
Chocolate (Lindt)	0.073
SPICES	
Capers (preserved in salt)	2.10
Capers (preserved in vinegar)	0.20
Pepper, black	0.51
Pepper, white	0.019
Mustard	2.66
Vanilla	0.055
Cinnamon	0.061
Cocoa beans	0.05—0.095
Coffee (roasted)	0.045
Tea	0.15
DRINKS	
Ground water	0.0012—0.0060
Spring water	0.00055–0.0046
Ale	0.0017
Beer (German)	0.016
Beer (English)	0.10
Champagne (Moët & Chandon)	0.0045
Apollinaris	0.043
Fachinger	0.039
Giesshübel (Mattoni)	0.0021
Vichy	0.053
FOODS PREPARED FOR TABLE	
Bouillon	0.5—1.0
Thick soups	0.54
Roast beef	0.98
Roast pork	1.54
Chops	0.97
Roast chicken	0.39
Sauces	0.7—1.5
Scrambled eggs (salted)	1.10
Spinach	0.91
Carrots	0.46
Cauliflower	0.49
Green salad	0.41
Apple sauce	0.031
Stewed pears	0.019
Tapioca pudding (unsalted)	0.026
Macaroni (à la Napolitaine)	1.04
Rice with apples	0.18

THE PURIN-FREE DIET

Purin bodies preëxist in the food and are formed within the body. The former are designated exogenous, the latter endogenous purins. Both animal and vegetable foods contain purins. Those of greatest interest to the physician are guanin, adenin, hypoxanthin, xanthin, uric acid, caffein (thein), and theobromin. The ingestion of exogenous purins raises the purin-content of the urine, and in proportion to the amount taken, but less is excreted than is ingested. The excretion of endogenous purins is essentially constant for each individual.

The use of the purin-free diet is based upon the theory that gout and some other disorders are dependent upon the retention of uric acid in the body. The diet has also been employed in diseases of the kidney, for some headaches, and "bilious attacks." Proof is lacking, however, that the diet possesses definite value.

PURIN CONTENT OF FOODS (Reckoned as Uric Acid)

According to Schmid and Bessau (37), Walker Hall (18), and Hesse (19)

100 Gms. Contain	Uric Acid Gms.	100 Gms. Contain	Uric Acid Gms.
Beef	0.111—0.189	Anchovy	0.465
Mutton	0.078—0.191	Oysters	0.087—0.217
Pork	0.123—0.185	Lobsters	0.066
Veal	0.114—0.189	Caviar	0.110
Ham (raw)	0.072—0.139	Cauliflower	0.024
Tongue (calf)	0.165	Spinach	0.072
Brain (pig)	0.084—0.233	Celery	0.015
Liver (beef)	0.279—0.372	Asparagus	0.024—0.057
Kidney	0.240—0.320	String beans	0.006
Thymus (calf)	0.990—1.308	Potatoes	0.006
Chicken	0.087—0.186	Mushrooms	0.015—0.019
Pigeon	0.174—0.154	Peas	0.054—0.079
Goose	0.099	Lentils	0.075—0.162
Venison	0.117—0.182	Beans	0.051—0.098
Bouillon	0.045—0.151	Oatmeal	0.064
Meat Extract	2.000—5.000		
Trout	0.213	The following foods contain no purins:	
Shellfish	0.117	Bread	Beets
Cod	0.067—0.131	Cereals	Onions
Salmon	0.072—0.201	Fruits	Port
Carp	0.162	Eggs	Sherry
Herring	0.207	Milk	Bordeaux
Sardines in oil	0.354	Cheese	

Purin Content of Beverages

According to Walker Hall (18) and Labbé (22)

100 Gms. Contain	Purin Bodies Reckoned as Uric Acid in Grams Chiefly Methyl-purins		
Coffee (roasted)	1.24	1 Cup tea (Ceylon) contains	0.0805
Tea	1.35—3.58	1 Cup tea (Indian) "	0.0700
Chocolate	1.43	1 Cup tea (Chinese) "	0.025—0.046
Cocoa	1.30	1 Cup coffee "	0.110—0.250
Beer	0.016	1 Cup chocolate "	0.268—0.572
		1 Cup cocoa (10 gms.) "	0.130

Purin Nitrogen Content in Per Cent.

From Vogel (48)

	Purin N.		Purin N.
Beef*	0.059	Oatmeal	0.030
Beef liver	0.099	Rice*	0.0004
Beef thymus	0.398	Potatoes*	0.001
Cod*	0.040	Spinach*	0.022
Wheat meal	0.001	Milk	0.0002
White bread	0.008	Swiss cheese	0.0004
White bread*	0.005	Egg	0.0
Hominy	0.004	Tomatoes*	0.0

THE INVALID'S DIETARY

Oatmeal Gruel (plain) (from *Food*).—Two tablespoonfuls of granulated oatmeal (45 grams, 184 calories), one saltspoonful of salt, one scant teaspoonful of sugar (8 grams, 33 calories), one cupful of boiling water, one cupful of milk (300 grams, 216 calories). Mix the oatmeal, salt and sugar together, and pour on the boiling water. Cook for thirty minutes; then strain through a fine wire strainer to remove the hulls, place again on the stove, add the milk, and heat just to the boiling point. Serve hot.

This gruel furnishes 425 calories.

Barley Water (Cautley).—(1) *Thin.* Put a teaspoonful of prepared or pearl barley, previously washed in cold water, into a jug, pour half a pint of boiling water on it, and add a pinch of salt. Stand it by the fire for an hour, stirring occasionally, and then strain through fine muslin.

Similar thin cereal decoctions may be made from rice, arrowroot, or oatmeal.

*Foods bought in America.

(2) *Thick.* Put a heaped tablespoonful of washed, prepared, or pearl barley into a clean sauce-pan and add a quart of water and a pinch of salt. Boil slowly until it has evaporated down to about two-thirds of a quart and strain. It may be flavored as desired. The addition of a little lemon peel, while boiling, is best.

The composition of barley water is:

0.09	per cent.	protein
0.05	per cent.	fat
1.6	per cent.	carbohydrate

It furnishes 14 calories to 100 c. c.

Toast Water (Cautley).—Pour a pint of boiling water over two or three slices of well-toasted bread. Let it stand until cool; strain.

The calory value of this preparation is negligible.

Chicken Broth (Bartholow).—Skin and chop fine a small chicken or half of a large fowl, and boil it, bones and all, with a blade of mace, a sprig of parsley, and a crust of bread, in a quart of water for an hour, skimming it from time to time. Strain through a coarse colander.

The composition of chicken broth is:

84	per cent.	water
10.5	per cent.	protein
0.8	per cent.	fat
2.4	per cent.	carbohydrate

It furnishes 56 calories to 100 c. c.

Chicken Jelly (Adams).—Clean a fowl that is about a year old, remove skin and fat; chop bones and flesh fine, place in a pan with two quarts of water; heat slowly; skim thoroughly; simmer five to six hours; add salt, mace, or parsley to taste; strain, and cool. When cool, skim off the fat.

The jelly is usually relished cold, but may be heated.

Data for estimating the calory value of this preparation are not available.

Beef Tea (Cautley).—(1) Mince one pound of lean beef, and add to it one pint of cold water and ten drops of dilute hydrochloric acid. Let it stand for two or three hours, with occasional stirring, and then simmer for ten to twenty minutes. Do not let it boil. Skim well.

(2) Mince one pound of lean beef as fine as possible, and pound it in a mortar with a small teaspoonful of salt. Add the meat and its juice to one pint of water at 170° F. in an earthen vessel, and stand it for an hour by the fire, stirring at times. Then strain it through muslin, taking care to squeeze all the juice out of the meat.

The composition of beef tea is:

92.9 per cent.	water
4.4 per cent.	protein
0.4 per cent.	fat
1.1 per cent.	carbohydrate

It furnishes 25 calories to 100 c. c.

Invalid Broths (Thompson).—To one pound of chopped lean meat, either chicken, mutton, or beef, add one pint of cold water; let stand in a covered glass fruit jar from four to six hours; cook for three hours in a closed jar over a slow fire, strain, cool, skim off the fat, clear with egg, season, and feed warm or cold.

These broths, except the chicken broth, possess essentially the same fuel value as beef tea.

Beef Juice (Bartholow).—Broil quickly some pieces of round or sirloin steak, of a size to fit in the cavity of a lemon squeezer previously heated by dipping in hot water. The juice should be received into a hot, colored (preferably red) wine glass, seasoned to taste with salt and cayenne pepper, and taken hot.

Beef Juice (Cautley).—Chop lean beef fine, or scrape with a fork or meat scraper to separate the connective tissue, and put it in a jar or cup, with a pinch of salt and enough cold water to cover it. Allow it to stand from one to six hours, and then squeeze well through coarse muslin. It may be given alone or mixed with other foods, warm or cold, but not hot. It should be warmed by heating the vessel in hot water.

Beef Juice (Ringer).—Take one ounce of fresh beef, free from fat, chop fine, and pour over it eight ounces of cold water; add five or six drops of dilute hydrochloric acid, and fifty to sixty grains of common salt, stir it well, and leave for three or four hours in a cool place. Then pass the liquid through a hair sieve, pressing the meat slightly, and adding gradually toward the end of the straining about two more ounces of water. The liquid thus obtained is of a red color, possessing the taste of soup. It should be taken cold, a teaspoonful at a time. If preferred warm, it must not be put on the fire, but heated in a covered vessel placed in hot water.

The composition of beef juice is:

90.6 per cent.	water
5.0 per cent.	protein
0.6 per cent.	fat

It furnishes 25 calories to 100 c. c.

Beef Pulp (Cautley).—Scrape a piece of raw lean rump or sirloin steak with a fork or meat scraper until as much as possible of the muscu-

lar tissue has been obtained, separated from the tendinous parts. Pound it in a mortar to a pulp, and then rub it through a fine sieve. Season with pepper and salt. It may be taken in the form of sandwiches, or rolled up into small rissoles and lightly grilled or fried.

Very little of the nutriment of the meat is lost in this process.

Egg Albumin Water (Watson).—Take the white of an egg (30 calories) and to it add twice its own volume of water and strain through muslin. This gives about three ounces of a clear solution, containing as much protein as is found in the average sample of commercial beef juice.

This fluid, added to home-made beef tea, makes a nutritive solution almost indistinguishable from beef juice and at a fraction of the cost.

Egg Albumin Water (Cautley).—Take the white of a fresh egg (30 calories) and cut it in numerous directions with scissors. Shake it up in a flask with a pinch of salt and six ounces of cold water. Strain through muslin.

It can be made with thin barley water, and cream or sugar added.

Egg-nog.—The following recipe makes a glass and one-half of egg-nog:

Egg, 1 large (60 grams)	80	calories.
Sugar, 1 tablespoonful (30 grams)	120	"
Whiskey, 2 tablespoonfuls	90	"
Cream, 7 tablespoonfuls	210	"

Add the sugar to the yolk of egg and beat until very light. Whip the white of the egg and then the cream until very stiff. Add the whiskey to the yolk of egg and sugar. Mix well. Add one-half the cream to this, then one-half the beaten white of egg, then the remaining cream, and finally the remaining white of egg. Mix lightly.

Egg-nog (Bartholow).—Scald some new milk by putting it, contained in a jug, into a saucepan of boiling water, but it must not be allowed to boil. Beat an egg with a fork in a tumbler with some sugar; add a dessertspoonful of brandy, and fill the tumbler with the scalded milk when cold.

This egg-nog will furnish about 300 calories.

Savory Custard (Anderson).—Add the yolks of two eggs to a cupful of beef tea, with pepper and salt to taste. Butter a cup or a jam pot, pour the mixture into it, and let it stand in a pan of boiling water till the custard is set.

This will furnish 150 calories.

Egg Flip.—Boil or heat thoroughly a teacupful of milk; beat the white of one egg to a froth. Pour the milk over the egg, stirring constantly. Add sugar to taste.

This will furnish 230 calories.

Caudle (Yeo).—Beat an egg to a froth; add a glass of sherry and half a pint of gruel. Flavor with a lemon peel, nutmeg, and sugar.

This will furnish 120—150 calories, according to the consistency of the gruel. If milk is used to make the gruel, it will have a higher value.

Boiled Rice (U. S. Army Hospital Recipe).—Rice, one ounce (30 grams); salt, 20 grams; water, 4 oz. *Directions.*—Put the salt and water into a stewpan. When boiling add the rice, previously washed thoroughly. Boil for ten minutes, or until each grain becomes soft. Drain it on a colander. Grease the stewpan with clarified drippings or lard. Put back the rice. Let it swell slowly near the fire, or in a slow oven, for about twenty minutes, until the grains are well separated.

Boiled rice furnishes 60 calories to 1 tablespoonful.

Rice Pudding.

Rice,	3 tablespoonfuls	(100 grams)	360 calories.
Milk,	1 quart		700 "
Salt,	1 pinch		

Wash the rice with water. Add to the milk and cook slowly on top of the stove for one hour, or a little longer, until the mixture becomes creamy.

Add

Sugar,	1 cup (280 grams)	1,148 calories.
Butter,	1 heaping teaspoonful	120 "

Cinnamon, nutmeg, or vanilla to taste.

Put into a dish to set and bake in an oven until the top is browned.

The whole pudding contains 2,325 calories. It furnishes five to six portions.

Rice Pudding (Cautley).—Cover the bottom of a dish with clean rice, nearly fill with milk, and add sugar; put it in a slow oven for three hours, and in the hottest part of the oven for fifteen minutes.

With the indefinite statement of the amounts of the ingredients, the calory value of this preparation cannot be estimated.

Rice and Egg Pudding (Cautley).—Take three ounces (90 grams, 315 calories) of rice and swell it gently in one pint of new milk (350 calories). Let it cool, and stir well into it one ounce of fresh butter (230 calories), two ounces of powdered sugar (240 calories), the yolks of three eggs (150 calories), and some grated lemon peel. Pour into a well-buttered dish and put on the top the whites of the three eggs (96 calories), beaten with three tablespoonsful of powdered sugar (185 calories). Bake for twenty minutes until lightly browned.

The whole pudding contains 1,550 calories.

Arrowroot (Pavy).—Mix thoroughly two teaspoonfuls of arrowroot

with three tablespoonfuls of cold water, and pour on them half a pint of boiling water, stirring well meanwhile. If the water is quite boiling, the arrowroot thickens as it is poured on, and nothing more is necessary. If only warm water is used, the arrowroot must be afterward boiled until it thickens. Sweeten with loaf sugar, and flavor with lemon peel or nutmeg, or add sherry, port wine, or brandy, if required. Boiling milk may be employed instead of water, but when this is done no wine must be added, as the milk would curdle.

Cocoa Junket.[1]

Cocoa,	1 teaspoonful	50 calories.
Milk sugar,	25 grams	100 "
Milk, 5 oz.,	150 c. c.	100 "
Junket tablet,	¼	
Cold water,	1 oz.	

Dissolve the junket tablet in the water. Mix the cocoa and sugar, add the milk, and heat lukewarm, stirring constantly; add the dissolved junket tablet, stir thoroughly, and leave in a warm place to set.

Soft Custard.

Milk,	1 cup (8 oz.)	160 calories.
Egg,	1	80 "
Milk sugar,	60 grams	240 "
Salt,	a speck.	
Vanilla,	2 to 3 drops.	
Caramel, made of granulated sugar,	3 tablespoonsful	20 "

Beat the egg slightly; add the sugar, salt, and hot milk slowly. Cook in a double boiler, stirring constantly, until it thickens a little (if cooked too long the custard will curdle, but may become smooth again if set in a dish of cold water and beaten at once). Flavor and cool.

To make caramel: Put the sugar in a pan directly over heat and burn until a very dark brown. Dissolve in hot water or milk.

Plain Junket or Rennet Custard.

Milk-sugar,	25 grams	100 calories.
Milk,	5 oz. (150 c. c.)	100 "
Junket tablet,	¼	
Cold water,	1 oz.	
Vanilla,	few drops.	

See directions for "Cocoa Junket."

[1] This and the following recipes were published in the *American Journal of Medical Sciences* for Jan., 1912.

Baked Custard.

Milk-sugar,	40 grams	160 calories.
Milk,	6 oz. (180 c.c.)	120 "
Egg,	1	80 "
Nutmeg or vanilla.		
Salt,	a speck.	

Beat the egg slightly; warm the sugar and milk, stirring constantly; add to the egg, strain into a custard cup, and flavor. Bake in a pan of water in a moderate oven until a knife, when cut into it, will come out clean (½ to 1 hour).

Bread Pudding.

Milk-sugar,	45 grams	180 calories.
Milk,	6 oz. (180 c. c.)	120 "
Egg,	1	80 "
Bread,	1 slice ⅜" thick, 20 grams	60 "
Butter,	½ oz. (15 grams)	120 "

Spread the bread with butter, and cut into squares. Beat the egg slightly; heat the milk and sugar, stirring constantly; mix with the egg and pour over the bread. Grate nutmeg over the top and bake the same as custard.

Vanilla Ice Cream.

Cream,	4 oz. (120 c. c.)	240 calories.
Milk,	2 oz. (60 c. c.)	40 "
Milk-sugar,	60 grams	240 "
Vanilla,	few drops.	

Mix the cream, milk, and sugar and heat, stirring constantly, until the sugar is dissolved. Then flavor, cool, and freeze.

Cocoa with Milk.

Cocoa,	1 rounding teaspoonful	50 calories.
Milk-sugar,	60 grams	240 "
Milk,	4 oz. (120 c. c.)	80 "
Cream,	2 oz. (60 c. c.)	120 "

Mix the sugar and cocoa; cook in the milk until dissolved. Serve with the cream.

Cocoa.

Cocoa,	1 heaping teaspoonful	50 calories.
Milk-sugar,	60 grams	240 "
Water,	½ cup, 4 oz.	
Cream,	3 oz. (90 c. c.)	180 "

Mix the cocoa and sugar, add the water, and boil for four or five minutes. Then add the cream, or use less and serve with whipped cream.

Coffee.

Milk-sugar,	60 grams	200 calories.
Strong coffee,	4–5 oz.	
Cream,	2 oz. (60 c. c.)	120 "

Milk-sugar may be used likewise to sweeten tea, which may be served with or without cream.

Lemonade.

Milk-sugar,	120 grams	480 calories.
Cold water,	7 oz. (210 c. c.)	
Lemon juice,	2 tablespoonfuls (or to taste).	

Boil the sugar and water two minutes. Add lemon juice to taste, strain, and cool. The white of an egg may be added if desired.

Orangeade.

Juice of 1–2 oranges,	100–200 calories.
Milk-sugar, 50–100 grams	200–400 "

Mix the orange juice and sugar and serve in a glass with cracked ice.

PROPRIETARY FOODS

A great variety of proprietary foods are manufactured. Practically all of them are made from common articles of diet, such as meat, eggs, milk, grain, etc.

Proprietary foods possess no special nutritive virtues, as is so often claimed, which are not possessed by the natural foods from which they are manufactured. Neither do they possess any medicinal value unless some drug has been added to them. Some proprietary foods are partially digested. The predigested protein foods have an unusual and often disagreeable taste, and for this reason fail to stimulate the "appetite juice." There is no evidence that predigested protein foods are more completely absorbed than natural foods. In fact, they are likely to cause digestive disturbances and diarrhea, as Voit long ago pointed out. Some of them contain alcohol, as much as 22 per cent. If such a food is given as the sole or principal article of diet, the patient is likely to be kept in a state of constant exhilaration or intoxication.

Carbohydrate proprietary foods are said to have been predigested when a portion or all of the starch has been converted into sugar (or sugars). They are neither more easily digested nor more completely absorbed than the sugar (or sugars) into which the starch has been changed. The proprietary carbohydrate foods in general possess greater nutritive value than the protein foods.

As Lusk has said, the chief value of proprietary foods lies in their taste—and this is not always pleasing. Some proprietary foods may be

useful at times in order to gratify a patient's desire for change of flavor. Some are useful for modifying other foods, especially milk. Few, if any, of them should ever constitute the sole article of diet, except for the briefest periods or under exceptional circumstances. On account of their peculiar taste, or because of the lack of adaptation of the digestive glands (cf. Pavlov), it is always difficult to give proprietary foods in sufficient quantity to meet the energy requirements of the body without causing disturbances of digestion. Another, and equally important, fact is that the absence of, or alteration in, the salts of proprietary foods has been observed to produce serious disorders of metabolism, especially in children.

The composition of various proprietary foods is given in the following tables:

ANALYSIS OF SOLID MEAT EXTRACTS*

Name	Moisture	Total Ash	Chlorin as Sodium Chlorid in Ash	Total Proteins†	Total Meat Bases
	%	%	%	%	%
Armour's Extract of Beef	21.66	20.46	5.47	27.51	9.52
Beef Extract, Swift & Co.	20.16	27.28	13.51	15.38	10.70
Beef Extract, Coin Special, G. H. Hammond Co.	12.39	31.68	13.25	15.01	13.14
Extract of Beef, Premier, Libby, McNeill & Libby	21.86	30.92	18.32	14.93	9.98
Liebig's Extract of Meat	21.14	21.03	3.11	30.50	11.92
"Rex" Brand Beef Extract, Cudahy Packing Co.	26.50	24.06	8.54	22.12	11.11

ANALYSIS OF FLUID MEAT EXTRACTS*

Name	Moisture	Total Ash	Chlorin as Sodium Chlorid in Ash	Total Proteins†	Total Meat Bases
	%	%	%	%	%
Beef Juice, Wyeth & Bro.	58.84	16.21	6.71	6.45	5.99
Concentrated Fluid Extract of Beef, Armour & Co.	57.75	17.23	8.27	6.76	5.18
Fluid Beef Jelly, Mosquera-Julia Food Co.	68.97	13.85	10.05	8.13	3.06
Fluid Extract of Beef, Cibils Co., Importers	64.63	16.13	11.38	10.25	4.24
Meat Juice, Valentine's Meat Juice Co.	57.64	10.26	1.77	5.63	6.05
"Rex" Fluid Beef Extract, Cudahy Packing Co.	55.99	16.99	8.48	7.00	8.21
Vigoral, Armour & Co.	49.94	15.91	7.02	10.75	6.30

*U. S. Dept. of Agriculture, Bureau of Chemistry, Bull. No. 114.
†The sum of insoluble and coagulable proteins, proteoses, and peptones.

MISCELLANEOUS PREPARATIONS (Meat Extracts, Juices, and Powders)*

Name	Water	Total Ash	Chlorin as Sodium Chlorid in Ash	Total Proteins†	Total Meat Bases
	%	%	%	%	%
Bouillon Capsules, Royal Specialty Co.	14.75	39.75	29.72	22.19	6.93
Bovril, seasoned	43.39	16.09	8.73	22.06	6.02
Beef Jelly, Mosquera-Julia Food Co.	27.82	17.31	8.39	28.63	9.24
Essence of Beef, Brand & Co.	90.93	1.34	0.09	5.07	1.34
Predigested Beef, H. K. Mulfurd Co.	91.69	0.18	0.01	1.19	0.69
Soluble Beef, Armour & Co.	30.15	14.55	5.21	37.76	6.68
Bovox Essence of Beef, The Bovox Co.	65.77	17.29	9.73	16.57	2.78
Johnson's Fluid Beef	47.22	9.80	4.37	31.75	3.87
American Brand Extract of Beef, American Beef Extract Co.	27.54	34.73	24.73	26.69	3.59
Bovinine Concentrated Beef, The Bovinine Co.	80.40	1.55	1.05	14.14	0.28
Essence of Mutton, The London Essence Co.	82.03	2.25	0.18	12.00	1.78
Liquid Food, Murdock Liquid Food Co.	86.09	0.65	0.20	10.69	0.25
Maggi's Bouillon	56.56	21.94	17.53	2.13	5.83
Peptonized Beef, Rose	45.13	3.52	1.63	22.20	9.89
Beef Extract and Vegetable Tablets, Armour & Co.	22.29	23.66	18.14	18.87	3.15
Leube-Rosenthal's Beef Solution	72.68	3.91	1.84	16.13	1.34
Malted Meat Extract of Beef, American Malted Meat Co.	8.61	7.87	3.48	9.82	1.40

The following table, giving the composition of meat juices prepared in the laboratory, illustrates the nutritive value of home-made as compared with commercial products. Bigelow and Cook* state that "meat juice prepared in the home or hospital . . . is far superior as a food to the commercial meat extracts and so-called meat juices."

MEAT JUICES PREPARED IN LABORATORY*

	Water in Juice	Ash	Chlorin as Sodium Chlorid in Ash	Insoluble Protein	Coagulable Protein
	%	%	%	%	%
Round beef, cold pressed	85.76	1.53	0.12	1.00	8.56
Round beef, pressed at 60° C.	90.65	1.36	0.15	4.25	
Juice extracted from sirloin steak by cold pressure	96.13	0.46	0.05	2.13	
Juice extracted from beef chuck by cold pressure after 6 hours at 60-100° C.	98.11	0.39	0.05	....	

*U. S. Dept. of Agriculture, Bureau of Chemistry, Bull. No. 114, 1908.
†The sum of insoluble and coagulable proteins, proteoses, and peptones.

Analysis of Infants' and Invalids' Foods

From Sutherland's System of Diet and Dietetics (slightly modified)

Most of the analyses, except where otherwise stated, are those given by the makers.

Name of Food	Water	Protein	Fat	Carbohydrates		Ash	Remarks
				Soluble	Starch		
	%	%	%	%	%	%	
Albany Food	8.60	9.50	2.10	79.40		0.40	Much unchanged starch.
Allenbury Food, No. 1	1.82	10.70	16.79	65.51	1.10	4.08	Analysis by Fresenius.
	5.70	9.70	14.00	66.85	....	3.75	
	83.30	1.56	2.30	7.20	....	0.60	Ready for use: Hutchison.
Allenbury Food, No. 2	2.24	10.23	14.94	67.54	1.24	3.81	Analysis by Fresenius. A malted meal plus No. 1 Food.
	3.90	9.20	12.30	72.10	....	3.50	
Allenbury Food, No. 3	3.00	10.33	1.05	22.21	62.91	0.60	Analysis by Fresenius. Partly malted wheaten flour.
	6.50	9.20	1.00	82.80		0.50	
American-Swiss Food	5.68	10.54	5.81	45.35	30.00	1.21	Much cane sugar.
Anglo-Swiss Food	6.50	10.26	4.91	46.43	29.48	2.02	Much cane sugar.
Bananina	9.50	4.10	0.40	84.00		2.07	A banana flour.
Benger's Food	5.27	12.18	0.91	3.95	76.39	0.96	A milk modifier. Much digested in preparing.
Carnrick's Soluble Food	5.17	16.69	5.53	28.11	41.50	3.00	Much unchanged starch.
Chapman's Whole Flour	8.40	9.40	2.00	....	79.30	0.90	A whole meal flour.
Cheltine Infants' Food	7.20	16.20	3.92	71.00		1.83	Contains much starch.
Cheltine Maltose Food	4.60	5.30	0.27	87.60	....	2.25	Fully malted.
Coomb's Malted Food	7.90	12.10	2.80	76.80		0.40	Much unaltered starch.
Cremalto	22.26	6.40	20.26	44.67		1.79	Cream and malt.
Diastased Farina	8.30	7.60	1.30	81.70		1.10	Carbohydrates said to be made soluble in preparation.
Dry Peptonoids, soluble	1.50	40.00	....	51.50		7.00	
Fairchild's Milk Powder	5.54	1.19	0.05	92.00	....	1.22	Practically milk sugar.
Falona	7.00	8.40	3.50	79.90		1.20	Cereals and a fat-containing bean.
Frame Food	7.62	13.69	0.44	22.33	54.96	0.96	Not so rich in minerals as claimed to be.
Franco-Swiss Food	4.43	13.00	3.70	46.09	30.86	1.42	Much cane sugar.
Horlick's Malted Milk	3.06	16.35	8.78	67.95	0.00	3.86	Holt, 5th ed., 1909. Desiccated milk, 50.0; wheat flour, 26.25; barley malt, 23.0; sodium bicarbonate, 0.75.
(ready for use) Chittenden	92.40	1.15	0.60	5.38	....	0.29	
Horlick's Malted Food	1.97	12.06	1.40	81.97	0.00	2.60	J. D. Henderson.
Hovis Babies' Food	3.70	7.70	0.20	86.60	....	1.82	Fully malted.
Hovis No. 2 Food	2.40	5.70	0.10	90.10		1.70	Starch, 7.5%.
Imperial Granum	11.50	10.91	0.64	5.73	70.22	1.00	

ANALYSIS OF INFANTS' AND INVALIDS' FOODS—Continued

Name of Food	Water	Protein	Fat	Carbohydrates		Ash	Remarks
				Soluble	Starch		
	%	%	%	%	%	%	
I. and I. Food	5.50	10.30	2.30	80.50		1.40	Mainly starch.
John Bull No. 1 Food	3.98	21.00	11.87	54.29	....	5.32	Maltose, 21.32; lactose, 29.42; dextrin, 3.55.
John Bull No. 2 Food	1.68	11.06	0.68	37.65	43.30	1.74	Maltose, 23.31; dextrose, 1.32; dextrin, 5.38; lactose, 7.65.
Kufeke's Infant Food	8.37	13.24	1.69	23.71	50.76	2.23	Made in Germany.
Lehmann's Vegetable Milk	24.40	7.50	24.60	41.80		1.50	Made from nuts and can be added to milk.
Loeflund's Cream Emulsion	24.32	8.23	15.32	49.43	....	2.60	A thick brown paste made from milk and malted wheat extract.
Maltico Food	2.36	16.07	11.80	65.89		3.88	Lancet analysis. Composed of milk and malted cereals; no starch.
	1.63	15.19	17.19	63.00		2.99	
Manhu Infant Food	8.80	8.70	5.60	75.90		1.00	Desiccated milk and malted cereals; much starch.
Mellin's Food	5.62	10.35	0.16	79.57	....	4.30	Analysis by makers. For modifying milk. It is a desiccated malt extract from wheat and barley.
Milo Food	3.81	14.34	5.50	58.93	15.39	2.03	Desiccated milk with maltose and dextrins, 27.36, and cane sugar, 25%.
Moseley's Food	10.84	14.78	1.84	21.76	49.06	1.72	Complete conversion during mixing.
Muffler's Food	4.76	15.19	5.10	72.42		2.43	Analysis by Stutzer and Richmond. Desiccated milk, powdered white of egg, wheat flour and lactose.
	5.63	14.34	5.80	27.41	44.43	2.39	
Neave's Food	5.03	13.20	1.70	4.71	74.27	1.09	Practically all starch.
Nestlé's Food	3.81	14.34	5.50	58.93	15.39	2.03	A milk modifier.
Nichol's Food of Health	11.90	7.70	1.70	76.90		1.75	Mainly starch.
Nutroa Food	6.80	15.90	10.30	66.00		1.00	Cereals *plus* peanut flour; hence the fat.
Opmus Food	10.90	9.10	1.00	....	78.60	0.40	A granulated wheat flour.
Ovaltine	3.30	12.01	1.98	76.70	2.57	3.44	A Swiss product.
Phosphatine, Fallières	5.85	2.35	1.92	56.68	31.98	1.22	Calcium phosphate, cane sugar and starch of potato, rice, arrow-root, sago, cocoa.
Ridge's Food	9.23	9.24	0.63	5.19	77.96	0.60	Mainly starch.
Robinson's Groats	10.40	11.30	1.60	....	75.00	1.70	Mainly oats, without husk.
Robinson's Patent Barley	10.10	5.13	0.97	4.11	77.76	1.93	Ground pearl barley.
Savory & Moore's Food	5.34	10.79	1.06	27.81	54.09	0.91	Wheat flour and malt; much grape and cane sugar.
	8.34	9.63	0.40	44.83	36.36	....	
Scott's Oat Flour	5.80	9.70	5.00	....	78.20	1.30	A fine oat flour. Cf. Groats.

Analysis of Infants' and Invalids' Foods—Continued

Name of Food	Water	Protein	Fat	Carbohydrates		Ash	Remarks
				Soluble	Starch		
	%	%	%	%	%	%	
Theinhart's Infantina	5.03	16.17	5.00	53.61	16.72	3.47	Desiccated milk, diastased cereals, lactose, and cane sugar.
Theinhart's Hygiama	4.75	21.22	10.05	49.10	11.33	3.55	More concentrated and a little cocoa added. The fat is partly cocoa butter.
Triticumina Food	8.60	12.50	2.20	75.70		1.00	Mainly starch.
Virol	11.66	6.43	19.72	61.61	....	0.58	The first analysis is the one given by the makers.
	24.04	4.16	10.75	59.25	....	1.80	
Wells & Richardson's Food	7.76	11.85	1.64	39.00	36.43	2.61	Partly malted. Contains much cane sugar and no milk.
Wheat Flour	9.02	7.47	1.01	5.66	76.07	....	
Wheat Flour, baked	7.78	....	0.41	14.29	67.60	....	
Worth's Perfect Food	2.40	11.10	2.00	83.50		0.50	
				SUGAR.			
Aylesbury Dairy Co.'s Humanized Milks, No. 1[1]	89.43	1.30	4.00	4.70		0.49	
Aylesbury Dairy Co.'s Humanized Milks, No. 2	88.30	2.20	3.60	5.20		0.57	
Paget's Perfected Milk Food	88.04	....	....	....	....	....	
Gaertner's Fettmilch	....	1.08	3.83	6.82		0.23	
Condensed Whole Milk	....	1.50	3.20	6.00		0.35	
Sweetened	24.06	9.36	11.28	52.28		2.13	
Condensed Skim Milk	29.23	10.73	0.64	55.69		2.63	
Wells, Richardson and Co. Lactated Food	6.95	9.56	0.42	29.65	51.38	1.04	
Charles Martin's Cardinal Food	8.18	10.50	0.35	8.35	71.76	0.86	
Eskay's Albumenized Food	1.70	7.25	4.95	58.65	26.47	0.98	A milk modifier.
Lacto-Globulin	9.85	71.44	0.65	11.65	....	8.36	
Wampole's Milk Food	3.35	14.18	7.10	71.30	....	2.64	
Wemalta	8.85	12.31	1.35	29.70	....	0.78	
Triangle Food	7.35	12.25	1.70	3.75	74.25	0.70	
English Milk Food, malted	5.75	8.38	0.70	30.30	53.95	0.92	
Christie's Food	3.70	6.50	3.05	35.65	50.10	1.00	
Wyeth's Prepared Food	3.00	14.69	1.30	68.30	7.21	3.50	
Baby's Own	6.55	9.63	1.05	22.80	59.39	0.58	Requires additions of varying amounts of milk.

[1] This and the following analyses are taken from Wiley, "Foods and Adulterations," Philadelphia, 1911.

TABLE OF SO-CALLED MEDICINAL FOODS[1]

	Glycerin and Undetermined Matter	Ash	% of Nitrogenous Matter (Nx6.25)	Carbohydrates		Alcohol		Average Recommended Adult Dose Per Diem in C. C.	Total Calories in Per Diem Dose*	Cost Per Diem to Supply 1,430 Calories
				Before Inversion	After Inversion	By Volume	By Weight			
1. Carpanutrine	28.45	0.93	4.28	4.22	5.34	15.5	12.5	60	78.0	$3.39
3. Liquid peptones	3.63	1.00	4.50	0.00	6.05	22.0	18.0	150	258.6	1.84
5. Liquid peptonoids	0.23	0.93	4.93	6.56	10.57	17.5	14.0	150	247.5	2.06
7. Predigested beef	3.40	0.18	2.38	4.29	4.37	19.7	16.0	150	212.0	2.13
9. Nutrient wine of beef peptone	14.97	0.23	0.64	11.67	15.43	21.5	17.5	100	188.8	1.79
11. Nutritive liquid peptone	1.02	0.84	1.86	12.58	12.89	23.0	18.8	120	232.1	1.47
13. Panopeptone	2.60	1.10	6.38	5.76	11.92	18.5	15.0	50	92.3	2.39
15. Peptonic elixir	3.21	1.55	2.54	11.40	11.46	18.8	16.5	90	157.2	1.72
16. Tonic beef, S. & D	12.91	1.61	3.40	1.48	2.36	14.9	12.0	50	55.0	3.25
18. Liquid peptone	0.44	0.87	1.81	0.55	0.55	14.0	12.0	90	85.4	3.34
19. Cow's milk (3.8% fat)	....	0.07	3.50	4.80	4.80	....	....	2,000	1,429.6	0.20

[1] Jour. A. M. A., 1907, XLVIII, 1612.

* Total calories per diem dose includes the calories of alcohol in the liquid medicinal foods and the calories of the fat in milk.

The economic aspects of proprietary foods are illustrated in Figures 1 and 2. The data concerning the natural foods were obtained for the most part from U. S. Department of Agriculture, Farmers' Bulletin No. 142, and though the prices of foods have risen since 1906, when the bulletin was published, the increases in cost do not materially affect the comparisons. The data concerning the proprietary foods were obtained in the following manner: Typical proprietary foods were purchased in the

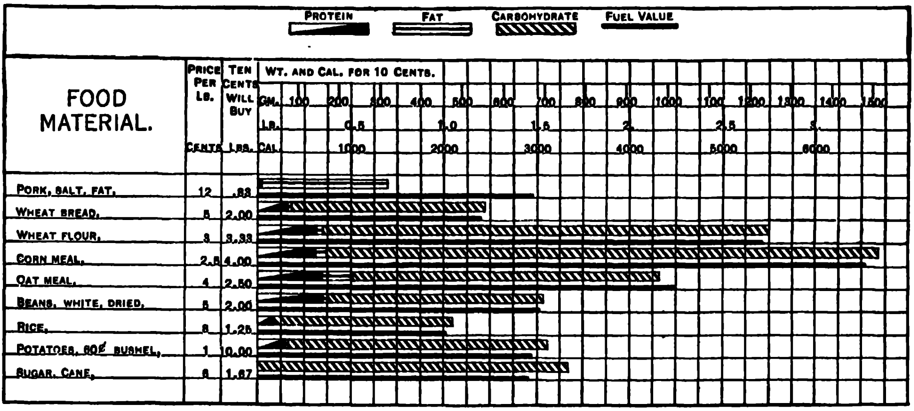

FIG. 1

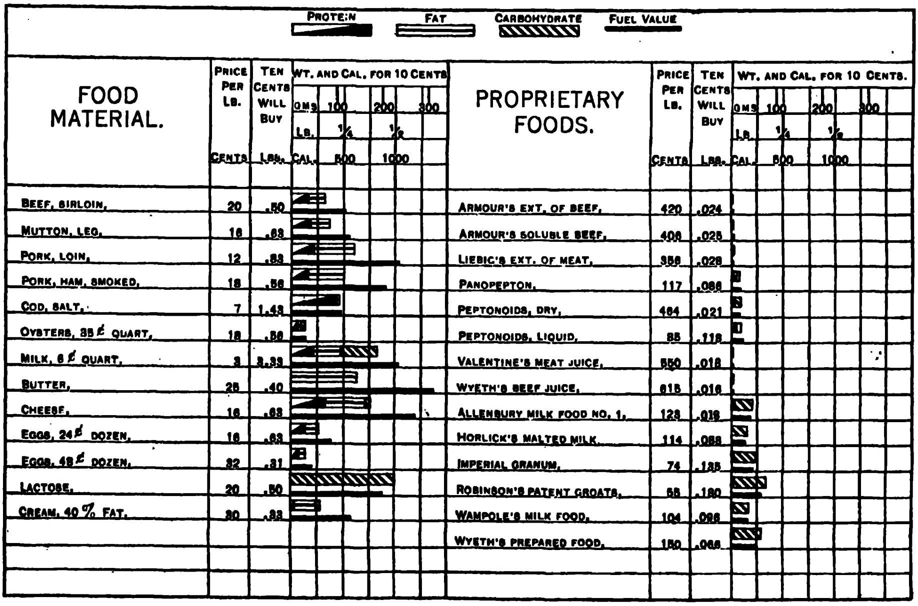

FIG. 2

FIGS. 1 AND 2.—SHOWING THE PURCHASING POWER OF 10 CENTS FOR VARIOUS NATURAL AND TYPICAL PROPRIETARY FOODS, EXPRESSED IN WEIGHT, AMOUNTS OF PROTEIN, FAT AND CARBOHYDRATE, AND FUEL VALUE.

open market, the contents of the packages were carefully weighed or measured, and published analyses of the foods were employed for plotting the values for protein, fat, carbohydrate, and calories.

A glance at the figures renders comment superfluous.

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CHAPTER XIV

TOXICOLOGY[1]

VICTOR C. VAUGHAN

INTRODUCTION

Definition and Action of Poisons.—Toxicology is the science of poisons, and includes the nature, occurrence, physical and chemical properties, action on living things, detection, and, indeed, everything pertaining to poisonous substances. In this article but little will be said concerning the chemical separation and identification of poisons. To do this would be to enlarge the subject beyond the space permitted the writer. It is not easy to define a poison. In fact, there seems to be more or less difference of opinion among toxicologists as to what substances should be included under the term "poison." Whether a given substance has a poisonous action or not depends upon the amount given, the method of administration, and the condition of the individual to whom the substance is administered. Taylor gives the following: "A poison is a substance which, when absorbed into the blood, is capable of seriously affecting health or of destroying life, and this as its usual effect upon the healthy body." Haines (25) thinks the above definition defective, inasmuch as quantity is not considered, and offers the following statement: "We may say, perhaps, in a general way that in the everyday affairs of life a substance to be regarded as poisonous must be capable of inducing harmful results if administered in doses of about sixty grains if a solid, or a teaspoonful if a liquid. This limitation, although somewhat arbitrary, is often of great convenience in the common use of the word 'poison' in the discussion of the subject in medico-legal cases." Kobert (36) gives the following definition: "Poisons are non-organized substances (inorganic or organic, artificially prepared or preëxisting in nature), which, by virtue of their chemical nature, under certain conditions so affect the organs of the body that the life or relative well-being of the body is temporarily or permanently seriously harmed." Other definitions might be given, but these suffice to show that recognized authorities do not agree. The fol-

[1] For other intoxications the reader is referred to Vol. II, Sec. II.

lowing definition is offered: A poison is a substance of definite chemical composition, which, by virtue of its constitution, is capable, when brought in contact with the tissues of the body, of modifying the cellular activity of one or more organs in such a way and to such an extent as to impair health or destroy life. In order that this definition may be understood it is desirable to say a few words concerning the structure and composition of the living body from the standpoint of the toxicologist. The lowest forms of life of which we have positive knowledge are unicellular. These cells in their essential parts at least are made up of definite chemical molecules. Cells grow by chemically combining with food elements. The metabolism that occurs within the living cell, and which is indeed the only constant and invariable distinction between dead and living matter, consists in the intramolecular absorption of new atomic groups and the simultaneous expulsion of old ones. Cellular assimilation consists in fitting the newly absorbed atomic groups into a molecular whole, and this is accompanied by a readjustment of the positions of the atoms. Cellular growth is due to polymerization, and cellular multiplication results from the cleavage or fission of the polymeric compounds. Nothing can serve as cellular food unless it combines chemically with some group within the molecule, and it is also true that nothing can act as a cellular poison unless it combines chemically with some group within the cellular molecule. Chemical germicides combine with atomic groups within cellular molecules, producing compounds which render the subsequent growth and multiplication of the cell impossible. The bodies of higher plants and animals are multicellular, and the life of the individual is the complex of the functions of its organs, which are made up of groups of specialized cells. Poisons are substances that impair or destroy cell function by chemical combination with certain groups within certain cell molecules. The cells of the different organs of the multicellular individual differ in their chemical composition, and consequently in their reaction with various chemical compounds with which they are brought in contact; consequently cell poisons have a selective action, some combining with red blood cells, some with connective tissue cells, some with liver, and some with nerve cells. All poisons are such by virtue of their effect upon the cells of the body, and the effect of a given poison upon the life and health of an individual depends upon the number and kind of cells whose function is interrupted. A poison which puts out of commission relatively few cells in the respiratory center of the brain, even temporarily, may cause the speedy death of the individual, while one that destroys thousands of red blood cells, or kidney or liver cells, may have no immediate visible effect upon the well-being of the individual as a whole, but the latter is as truly a poison as the former. This is an important point, and failure to comprehend it leads to failure to grasp the true significance of the word "poison." Among the unscientific there is a tendency to exclude

from the list of poisons all substances that do not induce an immediate and visible effect upon the health of the individual as a whole.

It will be evident from what has been said that everything that destroys cell life or impairs cell function cannot be classed as a poison, because it is only the substance that does this by virtue of its chemical constitution that can be so classified. A high temperature destroys all life, but temperature cannot be classified among the poisons. It destroys life by altering the chemical composition of the cells, in many instances at least, but not by virtue of its own chemical constitution, because it has none. A poison is a material substance of definite chemical composition, and not a mode of motion. Powdered glass when introduced into the stomach may mechanically destroy tissue, impair health, and cause death, and yet powdered glass is not a poison because its harmful effects are due to its physical properties and not to its chemical constitution. Our definition excludes from the list of poisons all substances whose harmful effects are due to their physical properties. Life may be destroyed by burns from hot air, water, or metal, but these are not poisons, because the ill effects induced by them are due to temperature and not to their chemical composition. It is sometimes inferred that every chemical compound is a poison if administered in sufficient quantity, and the scientific expert is frequently asked if common salt will not kill if taken in sufficient dose. It is true that the introduction of 15 to 20 c. c. of a 10 per cent. solution of common salt into the stomach of a rabbit will cause speedy death, and one-half pound in concentrated solution taken at once has been known to cause death in man, but we should distinguish between salt action and poisonous action. The concentrated salt solution kills because it rapidly extracts water from the tissues, and not because of the chemical reaction between the sodium chlorid and the constituents of the animal cell. The most inert chemical compound, and we know of none more inert so far as its effects upon the animal body may go than common salt, may kill if given by the mouth, or introduced into any cavity of the body, or injected into the blood in concentrated solution, but the effect here is due to the specific gravity of the fluid rather than to its chemical composition.

The medical witness is sometimes asked if it is not true that many of the remedies employed by him professionally are poisonous. This is true, and it is largely for this reason that the laws of all civilized nations regulate the practice of pharmacy and medicine, and throw about them such safeguards as are supposed to be necessary to exclude the ignorant and vicious from their practice. In the treatment of a grave disease, such as syphilis, the physician often prescribes, knowing that he must take the risk of doing more or less injury to the digestive apparatus or to the kidney, in order to save the central nervous system from the destructive effects of the disease. It is on account of the dangerous character of the tools he employs, and the great value and delicacy of the human body on

which he works, that the medical man demands that his profession be limited to persons of culture, skill, and integrity; and because he has prescribed borax or sodium sulphite not only without harm but with undoubted benefit is no reason why the butcher should be permitted to add either or both of these substances *ad libitum* to the daily food of his patrons.

While all poisons are such by virtue of their effect upon the cells of the body, it must not be supposed that this reaction is always a direct one, although it undoubtedly is so in many instances. The speedy action of certain poisons can hardly be explained in any other way than by direct action upon certain cells in the so-called vital centers of the brain, while, on the other hand, such poisons as ethylic alcohol, when taken in nonfatal doses through a long period of time, cause cirrhotic changes in the liver, and after a while these become so extensive that this organ cannot function normally, and the individual dies. Potassium chromate leads to lesions in the kidney and, as a consequence of this, other organs suffer. Potassium chlorate acts upon the red blood corpuscles, and if a sufficient number of these be destroyed the continued existence of the individual is impossible. Destruction of the cells that supply the digestive enzymes must sooner or later lead to the death of the individual. The concentrated acids and alkalies, also the salts of the heavy metals, cause extensive destructive changes, and may lead to gangrene.

Variations in the Effects of Poisons.—One and the same poison may show wide differences in the symptoms induced by it. Some of the most important conditions influencing the effects of a poison may be briefly stated as follows:

(1) *The Size of the Dose.*—The size of the dose may greatly alter the symptoms, even when the smaller amount is greater than the minimum fatal dose. The larger quantity may overwhelm the system, obscuring and even obliterating local symptoms that may be quite prominent with smaller doses. When a large quantity of arsenic is quickly absorbed, the gastrointestinal symptoms, usually prominent, may be wholly wanting, while the effects upon the central nervous system predominate. A small, but fatal, dose of morphin is usually characterized by narcosis, while a massive dose may lead to the most violent convulsions.

(2) *The Physical State of the Poison.*—The physical condition of the poison influences the rapidity and violence of its action. It seems probable that no substance can manifest a poisonous action unless it exists in solution, and when administered in solid form it must pass into solution before it can affect the cells of the body. It may be dissolved in the body slowly or rapidly. In the former instance it may fail altogether to exert any poisonous effects. If in solution, the strength of the dilution may materially modify its action. The mineral acids in concentrated form may destroy all tissues with which they come in contact, while the

same amount of acid highly diluted may be relatively harmless. Poisons may be modified by the vehicle in which they are administered. The vehicle may contain something that will hasten and intensify the action of the poison, or it may contain some ingredient that will retard and even neutralize its effect. Phosphorus administered in oils is more readily absorbed and affects the liver more promptly than when taken in aqueous suspension. The cyanids in acid media liberate hydrocyanic acid, which acts more promptly and violently than the salt.

(3) *The Avenue of Administration.*—As a rule, the more readily the poison finds its way into the circulating blood the more speedily does it act, and the smaller is the dose required to lead to a fatal issue. For this reason intravenous and subcutaneous injections are more quickly and surely fatal than the same substance in like amount given by mouth or rectum. Moreover, some poisonous bodies are rendered inert by the digestive fluids, or are not absorbed from the alimentary canal, but when introduced under the skin or directly into the blood stream, act with great promptness. Many of the potassium salts are harmless, or at least relatively so, when administered by the mouth, but prove most potent poisons when given intravenously. The venoms are destroyed in the alimentary canal and act as poisons only when introduced through the skin, or directly into the blood. Other substances, such as the oxids of arsenic, have at most only a local effect when given subcutaneously, but act more promptly and deadly when given by the mouth.

(4) *The Condition of the Recipient.*—The condition of the individual receiving the poison determines to some extent its effects. Usually poisons taken by the mouth when the stomach is empty are dissolved more quickly and act more promptly than the same substance taken in full digestion. The constituents of the food may form compounds with the poison which are not readily soluble. This happens when mercury combines with the proteins of the food in the stomach, and this may wholly prevent the corrosive action of the poison. The condition of the organs of elimination is also of importance in this consideration. A man with sound, active kidneys may survive a dose of morphin that would prove fatal to a nephritic subject. Then there is the matter of idiosyncrasy which is full of interest, but imperfectly understood. A therapeutic dose of quinin, or a bit of egg, or a delectable dish of strawberries may cause an individual to develop a scarlatinous rash.

Disposition of Poisons by the Animal Body.—The animal body makes many efforts, more or less effectual, to dispose of poisons, both those introduced from without and those generated within. Man and some other higher animals easily empty the stomach when the interior of that viscus is brought in contact with irritating and otherwise objectionable material. Moreover, a brisk catharsis is caused by many poisons, and by this means the life of the individual is often saved, and the injury done is speedily

repaired. The action of the liver on poisons absorbed into the portal circulation has been much discussed, and has been made the subject of several researches. The power of this organ to arrest or to destroy poisons has been both affirmed and denied. The researches of Roger appear to show beyond doubt that the liver does lessen the toxicity of at least some poisons. This is accomplished by diverse processes, depending upon the nature of the poison. The alkaloids when combined with bile acid, and the heavy metals, when combined with nucleic acid, become less soluble, and are held longer in the liver; consequently, the effect is lessened. Some poisons are converted into conjugate sulphates, and thus rendered practically harmless, and in this condition are eliminated through the kidneys. Phenol is thus disposed of, and, provided the amount is not greater than that which can be neutralized, no harm is done the organism. Other poisons are disposed of by being conjugated with glycuronic acid, glycocoll, methyl, carbamic acid, acrylic and mercapturic acids. Some poisons, such as the heavy metals, combine with the nucleic acid of the white blood corpuscles, and are then deposited in the bones and connective tissue.

Symptomatology of Poisons.—The physician should always be alert to recognize symptoms due to poisons that may be given with criminal intent, taken accidentally, or in some nostrum, or as an adulteration in food. The purpose at this point is to make a few general statements concerning the symptoms induced by poisons, leaving special features to be discussed in the sections devoted to the individual poisons.

(1) *Vomiting and Purging.*—When either of these suddenly appears in a healthy person, it is fair to suppose that the condition is due to some gastrointestinal irritant, or is premonitory of some acute disease. Poisons that induce acute vomiting and purging are numerous and of diverse origin. Such are the salts of the metals and bacterial poisons generated in the food before or after it is taken into the alimentary canal. The vomiting and purging vary in degree of intensity, and, as a rule, when they suddenly occur in persons believed to be healthy, it is unwise to attempt to thwart nature's efforts to cast out the irritating poisons, and it is better to assist with the stomach tube and intestinal irrigation.

(2) *Vasomotor Disturbances.*—Many poisons affect the vasomotor centers and lead to marked changes in the color of the skin, the action of the heart, and of respiration. The skin may be pale, or the natural redness may be markedly intensified, and urticarial rashes are frequent. A picture closely resembling scarlet fever may result from a gastrointestinal irritant, from a dose of quinin, or other relatively harmless drug.

(3) *Cerebral Symptoms.*—Illusions, hallucinations, and temporary delusions may follow large doses of salicylic acid, and convulsions are caused by strychnin. Stupor and coma may result from the narcotics, or may be due to alcoholism or cerebral hemorrhage.

(4) *The Temperature.*—The influence of poisons upon the tempera-

ture has not been closely studied. It has been stated that there is no known poison the primary effect of which is to markedly elevate the temperature. This is not true. In strychnin poisoning the temperature may be elevated several degrees, especially when taken while the body is in a tetanic spasm. Arsenic and antimony, and possibly other gastro-intestinal irritants, may cause an elevation of from one to two degrees. Close observation of the temperature in cases of poisoning is needed. Heat and cold sensations are due to vasomotor disturbances, and are not to be relied upon as a measure of the actual temperature of the blood. In severe poisoning the temperature often falls, and may go as low as 95°; in some cases still lower.

(5) *Pulse.*—In most cases of acute poisoning the pulse is quick and feeble, the extent to which this is true being determined by the degree of shock. However, those poisons that act directly upon the respiratory center may not materially affect the pulse, which continues with surprising regularity for some minutes after respiration has stopped.

(6) *Respiration.*—The most common effect of poisons on the respiration manifests itself in dyspnea, which may be due to mechanical obstruction, as in edema of the glottis, from the local action of a corrosive poison, or to paralysis, as in chronic lead poisoning, or to muscular spasm, as in poisoning with strychnin, or to direct action on the respiratory center, as is observed with some of the bacterial poisons. Cheyne-Stokes respiration marks the approaching termination of many cases of fatal poisoning.

(7) *Motor Disturbances.*—Some of these are so characteristic that they justify a positive diagnosis; such as the tetanus due to strychnin, the wrist drop due to lead, and the mydriasis due to atropin. Paralysis of the sphincters is frequent in fatal poisoning, but retention of the urine is common in poisoning with narcotics.

(8) *The Eye.*—Contraction of the pupil by morphin and its dilatation by atropin are well known. Yellow vision from santonin and red vision from duboisin may be mentioned, and blindness from wood alcohol is quite characteristic.

(9) *The Ear.*—The characteristic ringing in the ear due to quinin, and the buzzing caused by salicylic acid, and the intensified sense of hearing resulting from strychnin are familiar to medical men.

(10) *Speech.*—The peculiar speech of alcoholic intoxication and the roughened voice of belladonna poisoning, especially the former, are well known.

(11) *Sensation Abnormalities.*—Anesthesia, paresthesia, hyperesthesia, formication, pins and needles sensation, and other sense disturbances in the skin are probably always due to some form of intoxication. The neuritis of chronic arsenical poisoning has been sufficiently distinct and characteristic in numerous instances to lead to an investigation which has enabled clinicians to reach a correct diagnosis.

(12) *Skin Lesions.*—Acnes and fungoid sores may be due to long-continued employment of the bromids or iodids, while arsenical melanosis, and the peculiar condition of the skin known as argyria, due to silver, may be mentioned. Gangrene due to ergot is rarely seen in this country.

The Diagnosis of Poisoning.—The physician who diagnoses a case of poisoning, especially in attempted homicide, and as a result of such a diagnosis saves the life of the intended victim, is to be congratulated; while, on the other hand, the physician who mistakes poisoning for some disease, and thus permits a criminal to perpetrate his crime, as it were in the presence of the physician, puts himself, to say the least, in an awkward position. Unfortunately, instances of the former are much rarer than those of the latter. In most cases of attempted suicide the diagnosis of the physician when he is called in is easy, but there are many cases of accidental poisoning and few of criminal character that go to the physician, who fails to recognize the true cause of the trouble. In all suspicious cases the remnants of food, drink, or medicine, vomited matter, and the excretions should be carefully inspected, and, if this is not satisfactory or convincing, portions should be taken for microscopical and chemical examination. Marks of corrosives on the hands, lips, face, and mucous membrane of the mouth should not be overlooked, and the prick made by a hypodermic needle may possibly be detected. The vomited matter may reveal something of value from its appearance, odor, or reaction. Portions of poisonous plants or of undissolved poison may be seen in the vomit, and the odor of hydrocyanic acid, alcohol, formaldehyde, opium, and nicotin is quite characteristic, while in phosphorus poisoning the vomit may be luminous in the dark. The odor of the exhaled air may give a clew in either poisoning or disease. An examination of the urine is often of great service. The long-continued use of sulphonal or trional makes the urine the color of a rich Burgundy from the presence of hematoporphyrin, which may be more positively identified by the spectroscope. Antipyrin and fuchsin give a red urine; methylene blue makes it greenish. Fresh urine after santonin poisoning is normal in color, but on becoming ammoniacal, or on the addition of ammonia, it becomes bright red. Phenol and allied bodies color the urine dark green, the color growing darker as the urine stands exposed to the air. Hemoglobinuria may be due to large doses of quinin, or to the inhalation of the arsenid of hydrogen. Methemoglobinuria follows poisoning with potassium chlorate, and hematuria may be due to any irritant to the urinary passages, such as cantharides and turpentine. Brownish and greenish brown urine may be due to phosphorus, lead, or mercury. The urine has the odor of violets after turpentine, and that of hydrogen sulphid in cystinuria. Albumin in the urine may be due to poisoning with any of the heavy metals or with irritants that are eliminated by the kidneys. Microscopical and

chemical examinations of vomited matters and the excretions should not be neglected in suspicious cases.

From symptoms alone it is quite impossible to distinguish absolutely between certain diseases and the effects of certain poisons. Cholera and cholera morbus are due to the poisons produced by bacteria, and inasmuch as these are gastrointestinal irritants the symptoms resemble those of arsenic, antimony, and other poisons not of bacterial origin so closely that the most skilled cannot always distinguish between them. The effects of the narcotic poisons are closely simulated in coma from disease. The fact that a person while in perfect health is suddenly taken ill, and especially if this illness falls within an hour or two after the taking of food or drink, should always awaken the suspicion of poisoning. This suspicion is intensified if a number of persons, after partaking of the same food, are stricken about the same time. This happens more frequently when poisons have been generated in the food by bacterial infection, and seldom has any relation to homicidal intent.

The General Treatment of Poisoning.—Some general statements concerning the treatment of cases of poisoning will be made here, but special treatment will be discussed under the individual poisons. The first thing to do is to remove any portion of the poison that remains unabsorbed, and since most poisons are taken into the stomach this viscus should be emptied, and the best way to accomplish this purpose consists in the use of a stomach tube. There is some possible danger of perforating the esophagus or walls of the stomach with a tube after corrosive acids or alkalies have been swallowed, but, inasmuch as the chance of perforation from the corrosive is greater still, the tube should be employed. It is well to have a bone, wooden, or metallic ring on the tube in relieving the stomach of poisons, in order to prevent biting the tube or the fingers of the operator. Coma is not a contraindication to the use of the tube, neither is the fact that the poison was administered hypodermically, because, when thus administered, many poisons, both inorganic and organic, in part at least, reach the stomach. In coma the introduction of a large volume of cool water into the stomach serves as a cerebral stimulant. The fact that free vomiting has already occurred does not do away with the desirability of washing out the stomach, because vomiting is an ineffectual means of cleansing this organ, especially of insoluble poisons which adhere to the mucous membrane. Water is usually employed in washing out the poison, but some demulcent fluid or a solution of a chemical antidote to the poison swallowed may be preferable. The first washing should be preserved for microscopical and chemical examination. The washing should be continued until all the unabsorbed poison is removed. This can sometimes be determined by the appearance, in other instances by the odor, and, in others still, only by chemical tests. In case a stomach tube is not at hand, vomiting must be induced. The methods of doing this are numerous, such

as tickling the fauces, the administration of lukewarm water, tartar emetic, copper sulphate, or mustard. The last mentioned is to be found in every house, and a teaspoonful stirred into a glass of water is generally efficient. However, the most excellent emetic is apomorphin, given hypodermically, and every physician should carry this drug in tablet form. One or two c. c.'s of a one per cent. solution constitutes the proper dose.

While it is true that coma is not a contraindication to washing out the stomach, care should always be exercised in this procedure, and especially when the patient is in coma. Strassmann states that there are three known cases of rupture of the mucous membrane of the stomach, with fatal hemorrhage, in washing out this organ. One of these was due to a cancerous condition, and the others were cases of opium poisoning. In the two from opium poisoning the tears radiated from the cardiac end of the stomach, and were undoubtedly due to over-distention. There are other cases reported as due to the use of a sound, and spontaneous ruptures of the walls of a diseased stomach are not unknown.

The large intestine should be cleansed by high injections, and the administration of saline cathartics, calomel, or castor oil, after washing the stomach and intestines, is often wise.

In case of a sting or bite on a limb, temporary ligation and keeping the limb cold will delay absorption while the wound is cleansed and cauterized. However, the ligature must not be too long applied as gangrene may result.

The administration by the mouth or introduction into the stomach through the tube of substances that neutralize the poison is an important procedure. For caustic alkalies, some weak acid, such as vinegar, lemon juice, or citric acid may be used. On the other hand, for acids and acid salts weak alkalies, such as sodium bicarbonate, calcined magnesia, lime water, or a teaspoonful of wood ashes may be employed. Most of the acids are rendered inert when neutralized, but it should be remembered that the soluble oxalates are quite as poisonous as oxalic acid. The administration of alkali is of more or less benefit, even after partial absorption of acid and acid salts, inasmuch as the absorption of the alkali tends to restore the normal reaction of the blood. Furthermore, alkalies are beneficial after poisoning with chlorin, bromin, iodin, hydrocyanic acid, and potassium chlorate, and it is believed that methemoglobin may be partially changed back into hemoglobin by increasing the alkalinity of the blood, and the alkali acts as a diuretic, and increases elimination through the kidneys.

The corrosive poisons owe their corrosive properties to the avidity with which they combine with proteins. Therefore, if proteins are introduced into the stomach in time, they save the walls of that organ from the destructive action of the poison. The whites of three or four eggs dissolved in a quart of water make a highly useful agent for lavage of the

stomach after swallowing corrosive poisons. It should be clearly understood, however, that the metallic albuminates of poisons must not be left in the stomach. The protein has only neutralized the corrosive properties, and the substance remains a poison. Special neutralizing substances, such as common salt for silver and ferric hydrate for arsenic, will be discussed under the individual poisons.

For the alkaloidal poisons a solution of tannic acid, one to two grains to the ounce, or a strong decoction of green tea may be employed in washing out the stomach, the alkaloidal tannates being less soluble than the sulphates, acetates, etc., but it should be understood that the tannates must not be left in the stomach, for in time they will be absorbed. Oxidizing agents, such as a one per cent. solution of potassium permanganate, are of benefit in cases of poisoning with morphin and other alkaloids; also with phosphorus and hydrocyanic acids, because the oxidation products of these substances are less poisonous than the substances themselves. However, too much must not be expected from this kind of treatment, for there is often much organic matter in the stomach, sufficient to absorb the available oxygen. Suspensions of charcoal, either animal or vegetable, have been much praised in the treatment of alkaloidal poisoning. It is supposed that the charcoal which is administered in suspension, a teaspoonful of the powder to a glass of water, mechanically absorbs and holds the poison. It will do this to some extent, provided the charcoal has been recently ignited, and has been kept from the air. Otherwise it is of but little value, and, when used, the charcoal should be washed out of the stomach.

The inhalation of oxygen and artificial respiration are of great value when death from failure of respiration is threatened. The forcing of oxygen into the lungs with bellows after tracheotomy has been practiced in cases of morphin poisoning, and is not wholly free from danger. Stimulation of respiration with electricity is of value in narcotic poisoning.

The hypodermic or intravenous injection of heart stimulants, such as strychnin sulphate and the aromatic spirits of ammonia, may be employed in threatened failure of the heart. The application of heat with hot water bottles and abundant covering is not to be neglected when the temperature falls below the normal. The value of this treatment may be demonstrated experimentally on animals, and the writer has frequently seen guinea pigs recover after the temperature has fallen below 94° if placed in a warm room, while those left in the cold have died. However, it is not safe to place a man whose temperature is falling as a result of poisoning in a hot bath, for the superficial blood vessels suddenly dilate and the heart stops. He should be placed in bed, warmly covered, and hot water bottles placed about the extremities. The importance of keeping the head low in threatened heart failure is generally understood.

Transfusion and the intravenous injection of defibrinated blood work well in animals experimentally, but the operation is too delicate and too

complicated to be resorted to on the spur of the moment in the treatment of man. Ringer first proposed and successfully practiced the withdrawal of a given quantity of blood, and the subsequent intravenous injection of twice the volume of a solution of 7.5 per mille of sodium chlorid, and 0.25 per mille of calcium chlorid. Landerer has used a like solution, with the addition of 1 per mille of sodium bicarbonate. This procedure seems sensible and reasonably safe, provided the operation is carefully done. The withdrawal of the blood removes a portion of the poison, and the subsequent injection of the salt solution dilates the blood vessels, increases blood pressure, and hastens elimination through the skin and kidneys. The hypodermic injection of a large volume, one liter or more, of sterile salt solution is easily done, is safe, and may be beneficial.

The direct transfusion of blood as practiced by Crile (12) promises to be of service not only in hemorrhage, but in some instances of poisoning. The transference is made from the radial artery of the donor to any superficial vein on the arm of the recipient. The transference tube is so arranged that intima comes in contact only with intima, and the possibility of clotting, or the introduction of any foreign body, is avoided. Crile and Lenhart (13) have found direct transfusion effective in poisoning with illuminating gas in experiments on dogs, provided the transfusion be begun as soon as the heart stops, but it is not efficacious after the full stop of the heart in poisoning with chloroform or adrenalin.

The value of stimulating active movements and of inaugurating passive movements in the treatment of poisoning with narcotics is generally understood and frequently practiced. The patient is kept moving with an attendant on each side for support, and the limbs are rhythmically flexed and extended. Flagellations with cold, wet towels are useful. In all cases of narcotic poisoning the bladder should not be forgotten, and should be emptied with a catheter when necessary.

The employment of pharmacological antagonists, as atropin, in morphin poisoning, must be practiced, if at all, with caution, and will be mentioned in the sections devoted to the individual poisons.

CLASSIFICATION OF POISONS

(1) Mineral.—These may be subdivided into: (a) metallic poisons, (b) acids, (c) alkalies, and (d) inorganic gases. Many substances derived from the mineral world owe their poisonous properties to artificial changes to which they have been subjected. Thus, silver as found in nature is inert, but in the form of the nitrate it becomes active. The intensity of action of many of the mineral poisons is largely dependent upon the combinations in which they exist. Thus, while metallic arsenic is practically without poisonous effect, the oxids of this metal are highly

poisonous. While some of the phosphates and phosphites are injurious to the body when employed in large doses, their action is not comparable with that of the isolated phosphorus, in which form this element does not occur in nature.

(2) Vegetable.—These may be subdivided into: (a) alkaloids, (b) organic acids, (c) poisonous glucosids, and (d) poisonous vegetable proteins.

(3) Synthetic.—The synthetic chemist has demonstrated the fact, long denied, that the toxicological action of a substance is determined by its chemical composition, and we are now able to predict, under certain conditions, the physiological effects of a new body from a knowledge of its chemical structure, and this action can be modified by the substitution of one group of atoms for another. The possibility of thus building up new substances capable of inducing modified or radically different effects seems to be unlimited. This branch of chemistry is still new. Additional discoveries along this line will probably greatly advance our knowledge of the science of toxicology.

(4) Animal.—Under this head we may mention the venom of serpents, the secretion of certain fishes, the poisonous leukomains, etc. Some of these are not poisonous to the animal in whose body they are generated, but act harmfully upon the tissues of other animals; while others act injuriously when allowed to unduly accumulate in the organism in which they originate.

(5) Bacterial.—Such are the toxins of diphtheria, tetanus, and certain other infectious diseases. The bacterial poisons may be divided into: (a) basic poisonous products, or the ptomains, (b) the so-called bacterial toxins, and (c) the protein poisons.

MINERAL POISONS

Arsenic

Occurrence.—Metallic arsenic occurs in nature only in small quantities, and is generally prepared from arsenical minerals, in which it is found combined with silver, iron, cobalt, copper, and nickel. The sulpharsenid of iron, known as mispickel, or arsenical iron pyrite, and the arsenid of cobalt are the most important arsenical minerals. Both the sulphids, orpiment and realgar, are quite widely distributed in nature, and are obtained as by-products in the mining of silver, lead, and zinc. Arsenous oxid and the arsenates occur somewhat widely distributed, but in small quantities, in certain soils and waters. On account of its wide distribution, and the difficulty of wholly removing it, arsenic is found in small amount in many manufactured chemicals. Traces of it may be

detected in commercial acids, especially sulphuric and hydrochloric, in the sulphates, carbonates, and phosphates. It is difficult to remove all traces of arsenic from some of the metals and their salts. This accounts for the difficulty that has been experienced in securing zinc perfectly free from arsenic, and for the presence of traces of this substance in compounds of antimony, bismuth, and cobalt. It also explains the frequency with which traces of arsenic may be found in certain medical preparations, such as tartar emetic and bismuth subnitrate. Arsenical pyrite not infrequently occurs in bituminous coal. However, no harm has been known to result from the presence of arsenic in coal, and during the process of combustion it is completely volatilized.

In the Human Body.—There has been some difference in statement concerning the occurrence of arsenic as a normal constituent of the human body. The researches of Gautier (21) show that arsenic is occasionally, at least, found in the skin and its appendages, and it is the belief of this investigator that it is a normal constituent of these tissues. However this may be, it has no bearing on medicolegal investigation, since no chemist claims that arsenic exists naturally, even in traces, in the stomach, liver, kidneys, muscles, and other soft tissue. Moreover, the quantity found in the skin, hair, nails, etc., under natural conditions, is too small to be of significance to the toxicologist.

In the Soil.—The fact that the soil of graveyards frequently contains arsenic has given rise to much discussion and some experimentation concerning the possibility of a body buried in such a soil absorbing small quantities of this substance. Usually the arsenical minerals found in soil are insoluble in water, and when this is the case the chance of a corpse absorbing arsenic from the soil in which it is deposited is slight. For many years arsenical embalming fluids in which the arsenite of potash is the chief constituent were so extensively used that it is possible that the soil of many cemeteries has become impregnated with soluble arsenical preparations, and the possibility of a corpse absorbing arsenic from such soil must be admitted. Furthermore, it cannot be denied that there are soils which have never been artificially contaminated, and which do contain soluble compounds of arsenic. This is shown to be true by the frequent occurrence of arsenic in mineral waters.

Another way in which soil may become more or less impregnated with arsenic is to be found in the use of arsenical superphosphates as fertilizers. The arsenic contained in these preparations is slightly soluble, and may contaminate not only the soil and water, but may be taken up by growing plants, in which its presence may be detected. Moreover, the common use of Paris green for destroying insects on potatoes and other vegetables and for spraying fruit trees may lead to the contamination of the soil, and may account for the detection of traces of arsenic in turnips, potatoes, and other vegetables. In case only a trace of arsenic is found in a body that

has lain in the ground for some weeks or longer the prosecutor may have an analysis of the soil of the cemetery made, but when weighable quantities of arsenic are found in the body the possibility that the poison has found its way into the corpse from the surrounding soil is not worthy of serious consideration.

In Manufactured Articles.—Arsenic is extensively used in the manufacture of various articles, and it is well to call attention to some of its uses. In the preparation of the anilin dyes arsenic is employed, and it is not always entirely removed; consequently, traces of it may be found in the preparations placed on the market. The writer has seen several cases of severe irritation of the skin which he believed to be due to the presence of arsenic in red flannel underwear; at least, the examination of these garments revealed the presence of easily detectable quantities of arsenic, and the skin affections disappeared on leaving off the suspected garments and reappeared on their resumption. A similar case has been reported by Bourquelot and Galippe (4). About twenty years ago arsenic was frequently used in coloring wall paper, but this is no longer the case.

Arsenic is used not only in colored articles, but also in sizing letter paper. This fact is worthy of mention here, not because there is any likelihood that any one will ever be poisoned from arsenic in this way, but it is well for the toxicologist not to lose sight of this use of arsenic. It has happened to the writer to place pulverized zinc on a sheet of writing paper, preparatory to transferring it to a Marsh flask, and in this way contaminate the zinc with arsenic sufficiently to produce a well-defined mirror. A preparation quite extensively used in sizing letter paper consists of aluminium acetate, glycerin, and arsenous oxid. Arsenic is so widely distributed in manufactured articles that the toxicologist must always have this fact in mind in order to escape falling into error.

In Embalming Fluids.—For many years arsenical embalming fluids were almost universally used. Now, however, most states forbid this use of arsenic. In order to be safe it is always wise to test the embalming fluid, when such has been used, for arsenic.

In the Household.—There is probably no other chemical so generally used as a poison as arsenic. Rough on rats is arsenous oxid, in some instances, colored by an admixture of lamp black, though generally sold as pure white arsenous acid. The fact that this poison is so frequently found in the household, and can be so easily obtained, has led to numerous instances of both accidental and intentional poisoning with it. Paris green is largely used as an insecticide, and is sprinkled with free hands over vegetables and fruit. Its characteristic color prevents its frequent use for homicidal purposes, but perhaps intensifies the longing that the suicide seems to have for it. However, it is sometimes administered with green vegetables. Fly poison, consisting generally of powdered arsenid of cobalt, though sometimes of finely divided metallic arsenic, is an occasional

source of accidental poisoning. Arsenical soaps are in some sections of the country largely used for washing animals that show any manifestation of skin diseases, and occasionally individuals are poisoned by drinking from receptacles in which such soap has been carried. London purple, which is a waste product from anilin factories, is another form in which arsenic reaches the household, to be used for the destruction of pests of various kinds. Grape sugar may contain arsenic, and in some instances in large quantity. This is due to the presence of arsenic in the commercial sulphuric acid employed in the manufacture of sugar. When such sugar is used in the preparation of articles of food cases of arsenical poisoning may result. This is the explanation of the widespread outbreak of arsenical poisoning at Manchester, England, in 1901, which was traced to the use of arsenical grape sugar in the manufacture of beer, and in which more than 6,000 people were affected, and 70 died.

In addition to the uses above mentioned the quack doctor employs arsenical pastes for the removal of all growths denominated by him cancer, including any and every excrescence upon the person of any of his dupes.

Preparations.—Metallic arsenic is but little used except in the finely divided form known as fly poison. When pure its toxic effect is not great, and it easily undergoes oxidation, and is converted into highly poisonous compounds. Especially is this true when the metal is exposed to the air in the finely divided state.

Arsenous oxid is the preparation generally known as arsenic. It is prepared by roasting and subliming arsenical ores, and condensing the oxidized volatile products in hoods, or in chimneys arranged for this purpose. Arsenous oxid is found in the market in two forms, the white powder and the solid, vitreous mass. These are of the same chemical composition, and the difference in appearance is due to the fact that in the preparation the sublimed arsenic is sometimes deposited upon hot iron hoods, and is fused into a vitreous mass. This, when powdered and exposed to the air, becomes the white arsenic, which is the form most frequently seen. Arsenic is only sparingly soluble in water, and when mixed with it rapidly forms a deposit. At 15° C. the amorphous variety is soluble in water in the proportion of 1 to 108, and the crystalline 1 to 355. In boiling water the former dissolves 1 to 30, and the latter 1 to 46. It is readily soluble in both acids and alkalies, forming with the latter the arsenites and arsenates employed in medicine. It crystallizes in octahedra, which are easily recognized under a low-power microscope. It is practically without taste, although some find it sweet, or salty, or metallic. At any rate, the taste is not characteristic or pronounced, and this fact aids the criminal in its administration. The sulphids are but little used, and only indirectly concern the toxicologist. They are very feebly soluble in dilute hydrochloric acid, and when administered in granules may pass through the alimentary canal without harm. The most frequently used

medicinal preparation is a one per cent. solution of arsenite of potash, generally known as Fowler's solution, which, on account of its dilution, and from the fact that it seldom falls into the hands of any one outside of the medical profession, is rarely used for either suicidal or homicidal purposes.

Poisonous Action.—Arsenic is a universal poison to the higher animals, and so far as we know there is no vertebrate immune to its effects, although susceptibility varies within wide limits. For unicellular organisms arsenic apparently is not a poison, but many invertebrates are markedly susceptible to its action. Not only are all of the higher animals susceptible to arsenic, but it is poisonous to all kinds of tissues. It produces deleterious effects when applied to the unbroken skin, when it comes in contact with mucous surfaces, and when administered subcutaneously, and when inhaled in a gaseous form. When applied locally in sufficient quantity it causes necrosis of tissue, and when administered internally it will alter the composition of the blood, cause atrophy of the muscles, modify the growth of bone, and induce pathological changes in the nerves. Authorities are not altogether in harmony concerning the *modus operandi* of this poison. It is generally believed that it induces cellular death by its direct local effect as an irritant, and its corrosive action has been attributed to the avidity with which it is said to combine with proteins. But Binz and Schultz claim that there is no albuminate of arsenic, and that it has, properly speaking, no corrosive action. These authorities hold that the poisonous action of arsenic is due to the readiness with which it gives off and takes up oxygen. Arsenous acid is a reducing agent, while the arsenic compound is equally effective in causing oxidation. The above mentioned authorities show that various animal and vegetable substances at body temperature reduce arsenic acid to arsenous, and oxidize the latter to the former. Both of these processes are quickly wrought, both within and without the body. The sudden and continued withdrawal of oxygen from one molecule and its transference to another are believed by Binz to be the true explanation of both the therapeutic and toxic action of arsenic. He states that the most important lesions induced by arsenic are found in those tissues which are especially endowed with the function of receiving and utilizing the oxygen of the blood, such as the glandular protoplasm.

Symptoms.—The symptoms of arsenical poisoning are subject to wide variations, depending upon the form of administration, the amount given, the readiness with which it is absorbed, and the idiosyncrasy of the individual. On the one hand, it is unwise to deny arsenical poisoning, because certain prominent symptoms are absent and, on the other hand, it is equally unscientific to positively diagnose arsenical poisoning, even when the most typical symptoms are plainly developed. There are other forms of intoxication the symptoms of which cannot be positively distin-

guished from those of arsenical poisoning, and there are certain diseases which may closely simulate the action of arsenic. It should be plainly understood that, while the symptoms may justly cause suspicion, a positive diagnosis of arsenical poisoning, or its exclusion, cannot be predicated upon symptoms only, and in all cases which arouse suspicion the presence of this poison must be determined chemically before positive statements can be made. Roughly speaking, we can divide cases of arsenical poisoning into the following groups: (1) Acute; (2) subacute; (3) chronic.

Acute Poisoning.—When a large quantity of arsenic is taken into the stomach, or otherwise introduced into the body, the first symptoms generally appear within two hours, and consist of a sensation of faintness, generally referable to the region of the stomach. This is soon followed by nausea and vomiting, which frequently continue until death. The vomited matter first consists of any food material that may be in the stomach, then of mucus, generally stained with bile and sometimes streaked with blood. The vomiting is accompanied by a burning sensation in the stomach, dryness in the mouth and fauces, and marked thirst. Usually the vomiting is followed by severe purging, accompanied with tenesmus. The stools at first consist of the contents of the large bowel, and later become more choleraic in character, and are designated as "rice water." The continued vomiting and purging lead to symptoms of collapse, and the face becomes white, the lips blue, the eyes sunken, and the skin cold and clammy. Usually the patient dies within twenty-four hours, death being preceded sometimes by coma and convulsions. It will be seen that these symptoms resemble those of Asiatic cholera, and may be mistaken for violent forms of food poisoning. During the prevalence of cholera epidemics the physician may have great difficulty in distinguishing between this disease and arsenical poisoning and, indeed, he could do so only by the detection of the bacillus of the disease, or by the recognition of the poison. However, the difficulty that is most likely to arise is the differential diagnosis between arsenical poisoning and cholera nostras, and this difficulty is increased by the fact that this disease is not due to a specific microorganism. Therefore the physician must at first rely upon his suspicions, and subsequently upon the chemical demonstration of the presence of the poison. Arsenic may be detected in the vomited matter as a white powder, and identified microscopically and chemically.

In rare instances of arsenic poisoning the symptoms of gastrointestinal irritation may be largely or wholly absent. The patient immediately falls into a condition of collapse, with weak pulse and clammy skin, cold extremities, and coma or convulsions supervene and terminate in death. These symptoms are supposed to be due to the rapid absorption of the poison, and are more commonly met with when the poison has been administered in soluble form, although they may result from the introduction of large quantities of white arsenic into an empty stomach. Cases of this

kind have been known to terminate fatally in one hour, and Taylor reports a case with fatal termination within twenty minutes; but one or two cases of ultimate recovery have been reported. This is known as the narcotic type of arsenical poisoning.

In acute poisoning death invariably occurs within twenty-four hours; in the majority of instances within less than half this time, and it may happen in less than an hour. The mortality, even when prompt and proper treatment is employed, is about 50 per cent.

Subacute Poisoning.—When smaller quantities are administered, or when much of the poison is eliminated by vomiting, or neutralized by the administration of antidotes, the above mentioned symptoms come on more slowly, are less marked in character, and continue for a longer time. In cases of this kind vomiting is the most common symptom. There is pain in the stomach and over the abdomen, which is usually distended and tender to the touch. The skin becomes dry and warm, and sometimes is covered with a rash. Death usually occurs in from two to twelve days, although it may appear earlier, or be delayed, and it may be preceded by delirium or coma. In subacute cases it not infrequently happens that the vomiting ceases the second or third day, and there is apparent improvement, when a low fever, with dry tongue and rapid pulse, sets in, followed by cutaneous eruption, with mild delirium; death usually occurs in these cases from the sixth to the tenth day.

Chronic Poisoning.—Chronic arsenical poisoning is subject to great variation in the development and intensity of the symptoms. Frequently it is accompanied with some lesion of the skin. Arsenic rashes are for the most part of the erythematous type, but papules, vesicles, ulcers, pustules, and gangrene have been reported. The long-continued therapeutic administration of arsenic may be followed by pigmentation of the skin, which is generally most marked over the upper covered portions of the body, and may extend to the hands and face. The effects of arsenic on the skin have led to the supposition that the poison is eliminated through this avenue, and Brouardel and Pouchet have detected arsenic in the skin, nails, and hair of persons poisoned with it. Rarely there is observed a form of cutaneous pigmentation known as arsenical melanosis. This is due to the deposition of a nonarsenical decomposition product of hemoglobin in the skin. The epidermis becomes dark brown, and this color is, as a rule, most marked over the neck and extremities, although it has been observed in the axillæ and popliteal spaces. Microscopical examination shows reddish, brownish, or black granules about the lymph vessels of the papillæ, and in rare instances this pigment is deposited so abundantly that it forms small tumors. Chemically this coloring matter is identical with the bilirubin of the bile, and with the hematoidin crystals found in various parts of the body where there have been extravasations of the blood. While poisonous doses of every form of arsenic have more or less destructive action on the

coloring matter of the blood this effect is most marked when the poison is inhaled in the gaseous form. The urine becomes dark red, and even black, from the disintegration of the red corpuscles. Formed elements in the urine, such as epithelial cells and spermatozoa, may be stained brownish red or yellow. The broken-down hemoglobin is converted into bile pigment so rapidly that icterus is soon observed, and after twenty-four hours the skin may be quite thoroughly bronzed. Stadelmann studied the action of this poison on dogs with biliary fistulæ, and found that the amount of bilirubin was increased twenty times.

Arsenical paralysis may result from either acute or chronic poisoning, though more rarely from the latter, and from either internal administration or external application. There may be no evidence of it after large doses, and it may result from relatively small quantities. Why it appears in some cases and not in others has not been satisfactorily explained. Jaccoud thought it most common in alcoholics, but this has been denied by others. The paralytic affections vary in intensity from slight weakness to complete loss of motion, and they may be either transitory or permanent. They may set in with the first symptoms of gastric irritation or may be tardy, first appearing weeks after other symptoms have manifested themselves. Disturbances of motion are generally confined to the extremities, but there are some cases reported in which the muscles of the trunk have been involved. The four extremities are affected in most instances, but the legs are involved more frequently than the arms. Sometimes there is hemiplegia, but more often the paralysis is symmetric. It is most marked in the distal parts, the fingers and toes, and grows less evident nearer the trunk. Paralysis is always associated with muscular atrophy, which is characterized by its early appearance and rapid development. The atrophy may be degenerative or simple. Diminished response to faradic and galvanic stimulation is observed. The marked atrophy of the muscles of the extremities gives to the patient a peculiar appearance; especially in cases following acute arsenical poisoning it happens that the face and trunk appear quite healthy, while the limbs are shrunken. The subcutaneous fat on them disappears, and the nails become diseased and may fall out. The skin of the extremities is withered and dry except over the hands and feet, which are often bathed with cold perspiration. Sometimes there are ulcers. Edema is rarely observed. The tendon reflex is absent in all cases; the skin reflex has not been well studied. In some cases there are contractures, especially of the knee joint. These are due to unequal involvement of individual groups of muscles. Disturbances of sense accompany those of motion, and sometimes the former predominate. Pain is rarely absent, and in many cases it becomes the most distressing symptom. The histological changes which accompany these abnormalities of motion and sensation have not been closely studied. Popoff concluded from his experiments upon animals that arsenic induces a central myelitis, and that

the peripheral nerves remain unaffected; but more recent studies show that changes occur in the nerves and that arsenical polyneuritis does not differ from that induced by other toxic agents. There are proliferative changes in the neurilemma, and the inflammation may be exudative. Regeneration may occur, as it does after experimental division of nerves. Cases of paralysis of nerves not usually involved are known; such are the instances of anaphrodisia, reported by Biett, and later by Charcot; also of paralysis of the vocal chords observed by Mackenzie.

Post-mortem Appearances.—When an autopsy is held soon after death the skin is generally cyanotic, sometimes slightly icteric, and the body may be much reduced in flesh, even in cases of acute poisoning. The mucous membrane of the mouth, pharynx, and esophagus usually shows no abnormality. However, Husemann reports a case of aphthous formations on the lips and tongue and swollen uvula. Maschka describes a case of well-marked glossitis. In a large percentage of cases gastritis is more or less marked. Although the greater part or the whole of the mucous membrane of the stomach may be irritated, almost invariably there are areas in which the inflammation is deeper than elsewhere. The erosion varies greatly in intensity. It may be confined to the mucous membrane, or it may penetrate all the coats of the stomach and cause perforation. As long ago as 1753 Sproegel showed that these characteristic lesions result not only when arsenic is taken by the mouth, but also when it is absorbed from wounds; and since that time they have been frequently induced experimentally in the lower animals by the hypodermic administration of neutral solutions of arsenic. The pathogenesis of the gastric lesions has been a matter of some dispute among toxicologists. It has been generally assumed that the erosions are due to the local action of the poison; but, in view of the fact that they are produced by the absorption of arsenic when applied to raw surfaces, and follow hypodermic administration, Taylor and others have claimed that arsenical gastritis is a specific effect of arsenical poisoning, and is not due to local action. On the other hand, Virchow properly states that the gastritis of arsenical poisoning cannot be considered specific, for the same condition, with cloudy swelling, and a tendency to fatty degeneration in the glandular cells of the stomach are observed not only after poisoning with arsenic, antimony, or phosphorus, but also as a result of certain infectious diseases, such as small-pox. However, this explains nothing. It only gives a wider interest to the study of the pathogenesis of toxic gastritis. To say that the poison of small-pox induces in the stomach lesions similar to, or identical with, those induced by arsenic cannot be accepted as a satisfactory explanation of how the poison in either case causes these pathological changes. Moreover, it is altogether possible that the mode of action of the two poisons may be unlike, notwithstanding the fact that identical results are reached.

Binz and Schultz have endeavored to explain the gastric lesions in ac-

cord with their theory of the action of arsenic, which has already been given. They hold that in the alimentary canal there are certain "predilection" places in which the poisonous action of arsenic is most marked, and that the peptic glands constitute one of these localities. Böhm has suggested that the arsenical lesions of the stomach may be due to partial paralysis of the blood vessels of this organ. Hermann thinks it possible that arsenic may affect the peripheral nerves of the stomach, and thus indirectly so influence the local blood supply as to lead to inflammatory changes, and even to hemorrhagic erosions. Filehne found in some experiments upon rabbits that the gastric erosions do not occur when the contents of the stomach are kept neutral or alkaline, and he concludes from this that the lesions are due to self-digestion of the walls of the stomach; but he fails to explain how the arsenic makes self-digestion possible.

When applied *en masse* to the mucous membrane arsenic has a locally destructive action. Hoffmann reports a case which illustrates this nicely. He found a putty-like mass of arsenic in the stomach, and directly under it, of the same size and shape, an erosion. It is also true that arsenic administered hypodermically is eliminated by the mucous membrane, but it is difficult to believe that when thus given it can accumulate in sufficient quantity in certain small areas to cause severe and deep erosions. It will be seen, therefore, that the pathogenesis of the gastric lesions of arsenical poisoning must be left without satisfactory explanation for the present.

In cases where a large amount of white arsenic has been given by the mouth close inspection, especially with a magnifying glass, may reveal undissolved particles of the poison. When the examination is made some days after death yellow spots may sometimes be found in the stomach or large intestine, or in both. That these colorations are due to the sulphid of arsenic has been affirmed by some and denied by others. In several instances the writer has, by analysis, detected arsenic in these yellow spots. Brown and Davies examined similar stains in the stomach and intestines, and found only traces of arsenic; and conclude that the coloration was due to some decomposition product of the bile pigment. However, the evidence adduced from this conclusion is open to criticism. Frequently the wall of the stomach or intestine is stained through so that the coloration may be seen on both the mucous and serous surfaces. Hoffmann has shown that the sulphid of arsenic may be formed in the body as early after death as two days. He points out the fact that knowledge of the formation of this compound so soon may be of great importance, since realgar and orpiment may be employed in suicide, but neither would likely be used with murderous intent. His experiments enable him to state positively that the finding of the sulphid in the alimentary canal two days or longer after death is no proof that the arsenic was taken in this form.

The mucous membrane of the stomach may be thickened, and at certain points it may be stained with blood, and on attempting to wash these

stains away it will be found that the mucous membrane has been detached from the subjacent tissue, and is also removed. In some instances deep necrotic changes may be observed. Even when macroscopic lesions are not detectable there is an infiltration of the tissue, with round cells, a condition which has been designated by Virchow as gastroadenitis arsenicalis parenchymatosa. The upper portion of the small intestine may show alterations similar to those observed in the stomach. Multiple ecchymoses may be found along the intestinal tract. The contents of the small intestine are often thin and watery, and similar to the rice water stools of cholera. The solitary follicles and Peyer's patches may be markedly infiltrated. The alterations in the large intestine may be slight or more apparent. Frequently the epithelial layer is removed from areas more or less extensive, and the mucous membrane is infiltrated with white blood corpuscles. In animals the above mentioned changes in the alimentary canal may be observed, according to Pistorius, within two or three hours after subcutaneous administration, and within forty minutes after intravenous injection.

Histological Changes.—The lesions induced in the liver and kidneys by arsenic are for the most part microscopic. Only in exceptional instances has fatty degeneration progressed so extensively that it can be recognized by the unaided eye. Ziegler and Obalowsky have made a histological study of these organs, and the following statements indicate their findings: Fatty change in the liver cells is never absent, and is characterized by small drops in the protoplasm. The fatty changes seldom involve any large portion of the cells, but there are exceptions to this, and in some instances the alterations are as marked as in phosphorus poisoning. In many instances the fatty change is the only detectable alteration, but in others there may be cloudy swelling and increase of individual cells. The nuclei often stain imperfectly, or fail to stain altogether. Granules staining with saffranin may be seen in the protoplasm, showing that the nuclei have been broken down. Sometimes individual cells are seen to be shrunken and homogeneous, appearing brown in stained preparations, and showing colored granules instead of nuclei. That the cells involved in some of these alterations are still capable of multiplication is shown by the observation of typical karyokinetic figures. It may be remarked in this connection that in the examination of the liver of rabbits long under the influence of arsenic one gets the impression that the number of double nuclear cells is greater than normal. These proliferating cells may be observed in different parts of the acini, and it cannot be said that they have any local relation to any necrotic foci.

Most of the Kupffer cells are filled with fat drops, and in poisoning of short duration fatty changes are often more advanced in these than in other cells. Fatty changes in the intraacinous capillaries are seen here and there. These may be observed in animals which have been treated with

arsenic for only two days, but the best examples are found after from eleven to seventeen days. As proliferative phenomena there are observed swelling of the endothelial nuclei, increase of chromatin, and the appearance of typical karyokinetic figures. The proliferating cells are sometimes round, and sometimes they put forth processes which cross the lumen and attach themselves to the opposite wall of the capillary.

The periportal connective tissue is often found to be in a state of proliferation, which is indicated partly by the presence of more or less abundant karyokinetic figures, partly by the increase of cellular elements, and by the presence of numerous cells with large nuclei and rich in protoplasm. These changes can be seen in animals which have been only two days under the influence of the poison, but they become more marked after two or three weeks.

In the epithelium of the bile ducts there is a multiplication of the cells simultaneously with the proliferation of the connective tissue. After poisoning of long duration there often appears to be a formation of new bile ducts. However, the number of bile ducts in the periportal tissue of rabbits is normally so great that a positive statement on this point cannot be made. Changes strictly attributable to an inflammatory condition are not prominent. However, single leukocytes are observed in the proliferating areas, and sometimes the intraacinous capillaries contain many leukocytes. In point of time or place the proliferation shows no recognizable dependence upon the degeneration.

In acute arsenical poisoning hemorrhagic spots may be found not only in the alimentary canal, as has been stated, but also in the muscles, pancreas, lungs, and in serous membranes, and in the endocardium. The presence of ecchymoses in the endocardium of the left ventricle is frequently observed, and is regarded by some as pathognomonic of arsenical poisoning. However, similar ecchymoses may result from violent retching, due to any cause, and are common after death from failure of respiration. In chronic arsenical poisoning fatty changes may be observed not only in the organs mentioned, but also in the muscles, including those of the heart and diaphragm, and in the mesenteric glands.

Poisonous Dose.—The extent to which arsenic is tolerated varies markedly in different individuals, and it is impossible to make any exact statement concerning the amount necessary to produce injurious effects. In some persons arsenic apparently has a cumulative action, although this is the exception and not the rule. In such instances small doses continued for relatively short periods may produce evidences of chronic poisoning. Thus, Putnam (60) mentions a case of arsenical neuritis which was induced by the administration three times a day of four or five drops of Fowler's solution, continued for a month. However, there must be thousands of cases in which this and even larger amounts have been given for longer periods without ill effects. Usually one half grain of white arsenic

is sufficient to cause retching and vomiting in adults, and two grains, possibly less, may cause death. A case is reported in which a woman took about one half an ounce of Fowler's solution in divided quantities during a period of five days, and died on the fourth day after the last dose. It must be evident that the condition of the individual and the form in which the poison is administered have a large share in determining its effects. A common claim of the defense in trial for arsenical poisoning is that this poison is cumulative, and when given in medicinal dose it may accumulate in the stomach or other organ, and an attempt is made to account for the amount found by the chemist in this way. The writer has known a physician to swear that the more than two grains of arsenic found in the stomach by the chemist could be thus accounted for. It should be stated that this is impossible, and the claim is a subterfuge on the part of the lawyer, and an evidence of either venality or ignorance on the part of the man who claimed to be a medical expert. Arsenic, when given in medicinal doses, cannot accumulate in the body without inducing symptoms until a fatal quantity is stored up, and then suddenly kill. In fact, there is no poison that will act in this way, and in this sense there are no cumulative poisons. The words "cumulative poison" have too frequently been used by shrewd lawyers for the purpose of creating a "reasonable doubt" in the minds of the jury, and the medical man who aids in this deception is no credit to his profession.

Arsenic Eating.—Much has been said concerning the habit of eating arsenic, but, so far as we can learn, this is not a practice followed to any appreciable extent in this country. Pellew (56) mentions a case tried in Delaware County, New York, in 1861, in which it seems to have been shown that the deceased, who was a hostler, had this habit; and the same author states that a physician reported one case among the demi-monde of New York, and that he believed others of the same class indulge in this practice. Certain German authorities tell big stories of arsenic eaters in Louisiana, who are said to be immune to all infectious diseases. These so-called Arsenikophagites are designated as "dippers," and we are inclined to the belief that our Teutonic cousins have either confounded snuff dipping with arsenic eating, or have been listening to fairy stories. In the Maybrick case, which for so many years attracted attention both in England and in this country, it was claimed by the defense that the victim was an arsenic eater. However, the evidence on this point depended solely upon the testimony of a colored servant whose story was not worthy of belief. During the first part of the 19th century several articles were published in Austria describing the Arsenikophagites, or arsenic eaters, of Styria. It was stated that the mountain climbers of this region acquired the arsenic habit for the purpose of improving their appearance, of increasing their strength, and as a health preservative. This matter was investigated in 1864 by Maclagan (50), who found a number of arsenic

eaters and was convinced that the previous reports were true. Maclagan administered weighed quantities of arsenic to some of these individuals and detected its presence in the urine. It was found that most of these people ate orpiment, but they were quite ready to swallow white arsenic as well, having no preference for the yellow compound, and resorting to its use solely because it was somewhat more easily obtained. To what extent arsenic is now used in Styria we do not know.

Treatment.—The treatment of acute arsenical poisoning in order to be effective must be prompt and thorough. If a stomach tube is at hand it should be used, because this method of washing out the stomach is more effective than that of resorting to emetics. The washing should be frequently repeated, and it is well to use dilute solutions of sodium bicarbonate, because white arsenic is more soluble in dilute alkali than in water. The large intestine should also be thoroughly washed. This is best accomplished by passing a rectal tube up as high as possible, and thoroughly flushing the colon. When the stomach tube is not at hand reliance must be placed upon emetics. Tickling the fauces with a finger may be resorted to immediately, and later warm water and mustard should be freely used. Emesis is more complete when induced by sulphate of zinc, tartar emetic, or apomorphin. It should be borne in mind that crystals of white arsenic or Paris green adhere most tenaciously to folds of the mucous membrane, and every effort should be made to thoroughly dilate the stomach while washing it out. This is one of the reasons why the stomach tube is more efficient than vomiting. Through the tube water can be poured in until the stomach is distended, and when this is done the probability of thoroughly removing the arsenic is increased. The physician called upon to treat a case of acute arsenical poisoning must realize that the work of cleaning out the stomach and large intestine should be most thoroughly done. After the stomach has been washed several times with a dilute solution of sodium bicarbonate a large amount of ferric hydrate should be administered. This may be prepared by treating a solution of ferric chlorid or sulphate with an excess of ammonium hydrate, or sodium bicarbonate, and straining through a cloth. The precipitate is the portion administered. If a solution of ferric sulphate can be precipitated with magnesia filtration is not necessary, and the precipitate, suspended in the fluid, may be administered in this form. Magnesia is preferable to ammonic hydrate, for the reason that when the latter is added the precipitate must be removed from the menstruum in which precipitation has been induced; otherwise harm might come from excess of ammonia. When magnesia is employed an actual benefit may be secured from the sulphate of magnesia by its action as a purgative. Furthermore, magnesium hydrate is itself a chemical antidote to arsenic, scarcely inferior to ferric hydrate, and a mixture of the two is preferable to either used singly. In any case it is better to wash out the stomach two or three times after the antidote has

been administered, but after each washing a new portion of the antidote should be given. Ferric hydrate is inert, and there is no danger of administration in too large quantity, but the physician must bear in mind that ferric hydrate combines with arsenical preparations slowly and somewhat imperfectly, and for this reason thorough washing of the stomach and intestines should never be omitted, should always precede the administration of the antidote, and should be repeated several times after its administration. Both Paris green and white arsenic are removed with equal difficulty from mucous membranes, and too much reliance must not be placed on the antidote. Indeed, animal experiments fail to show much benefit in the use of these chemicals. After the stomach and large intestines have been cleansed as thoroughly as possible a purgative of some kind should be administered for the purpose of clearing out the contents of the small intestines which cannot be reached by irrigation. Either castor oil or a saline purgative may be used for this purpose. In most cases of chronic arsenical poisoning recovery, partial or complete, provided that histological changes are not too far advanced, follows the discontinuance of the use of the poison.

Several investigators have attempted to prepare an arsenical antitoxin serum, and at one time Besredka believed that he had been successful, but subsequent studies have shown that this was an error.

Unusual Forms of Poisoning.—The external application of arsenic, especially to abraded surfaces, may lead to either acute or chronic poisoning. In 1878 seventeen children in a foundlings' hospital in England were killed by the use of a chafing powder which contained nearly 40 per cent. of white arsenic. Cancer doctors sometimes cause acute poisoning, and even fatal results, by the application of arsenical ointments to ulcers and other sores. Criminal poisoning has been accomplished by the introduction of arsenic into the rectum or the vagina.

ANTIMONY

Occurrence.—Antimonial ores are widely distributed in nature. The most important is stibnite, known as black sulphid, in which form antimony has been employed from prehistoric times. The women of the oriental races used it as a cosmetic, as is shown by references in both sacred and profane literature. The question concerning the origin of the name antimony is one which has been much discussed and differently answered. It is most likely of Arabic derivation, but there is a story told concerning this name which is more interesting, if not so true. Basal Valentine was a German monk of the 15th century, who spent the greater part of his time as an alchemist. He certainly did investigate some of the preparations of antimony, and wrote a treatise laudatory of the medicinal value of the compounds of this element. The title of the book, *Currus triumphalis*

antimonii, is sufficient to indicate the style in which it was written. According to the story, this old monk threw some of the material upon which he had been at work to some hogs kept at the monastery, and observed that although some of these animals were somewhat violently purged by these preparations they speedily recovered and afterward grew sleek and fat. Thinking that a preparation which had proved to be so good for hogs might also be of value to monks, he is said to have fed some of his preparations to his brothers in the monastery, and as a result of it all died. Valentine then decided to call this substance anti-monk, which has since been corrupted into antimony.

Paracelsus loudly proclaimed the medicinal virtues of the antimonial preparations, and their abuse became so frequent that in 1556 the medical faculty of Paris decided that no reputable physician should use them, and they were condemned as poisons. Undoubtedly at that time tartar emetic was so largely used for criminal purposes that the reputable part of the medical profession decided not to employ it in any form. However, in later years, after the stigma had been removed, its use by regular practitioners was again countenanced, and antimony, especially tartar emetic, has continued among the pharmacopeial preparations down to the present time, although it is now but seldom used.

Preparations.—Metallic antimony is a grayish white substance, practically non-poisonous and incapable of oxidization at ordinary temperatures. When heated it is converted into the oxid, which resembles the corresponding compound of arsenic. The sulphid is occasionally used in veterinary medicine, but otherwise it is seldom seen. The chlorid, also known as butter of antimony on account of its color and consistency, was once quite extensively used for local applications and as a bronzing fluid, and cases of accidental or intentional poisoning with it occasionally occurred. Tartar emetic, or the double tartrate of antimony and potash, is prepared by heating the oxid with cream of tartar. It forms a white crystalline powder which is soluble in twelve parts of water at 20° C., and in three parts of boiling water. This is the form in which antimony is now most frequently found. However, its medicinal use has greatly decreased within the last thirty years. It was formerly employed both as an emetic and purgative, and was also much esteemed as an expectorant, and it figured as a constituent of certain household remedies, such as "Hive syrup." In the arts tartar emetic is now extensively employed as a mordant, and its presence in articles of clothing occasionally gives rise to certain skin affections. Commercial tartar emetic may contain traces of arsenic. When heated on charcoal globules of metallic antimony are formed along with an incrustation of the white oxid. Heated in a reduction tube it blackens and yields carbon and the metal.

Poisonous Action.—The double tartrate acts so violently as an emetic and purgative that when administered even with criminal intent and in

large doses the most of it is expelled from the body without serious harm to the individual. The purging after large doses is severe, and the discharge of rice-water stools abundant. Blood may appear in both vomit and stools. In its effects antimony, if possible, presents a clinical picture more closely resembling that of a severe form of Asiatic cholera than is seen in arsenical poisoning. Upon the mucous membrane of the alimentary canal the action of antimony differs from that of arsenic most notably in the appearance of aphthous patches in the mouth, esophagus, and stomach. Indeed, the local effect of arsenic is less marked than that of antimony. Schmiedeberg accounts for this on the ground that preparations of arsenic are absorbed more readily than those of antimony. It is on account of its marked local irritation of the stomach that antimony, acting reflexly, becomes the powerful emetic that it is. The lesions produced in other organs by antimony are practically identical with those induced by arsenic.

In fatal cases collapse may come on early, and may be most profound. The pulse becomes rapid and weak, the face ashy pale, the eyes sunken and glazed, the skin cold and clammy, and death may result from exhaustion, or it may be preceded by wild delirium or severe convulsions. However, recovery, even after marked collapse, is not impossible. Some years ago four women were employed during the vacation to scrub the floors of the writer's laboratory. On the first day they found a large bottle of sherry wine, which they proceeded to exhaust, and at the same time make themselves merry. The next day they found a large bottle of wine of antimony, and, doubtless presuming that this was only another brand of good wine, they proceeded to empty this bottle. The writer found them prostrated, and it was quite evident that each had vomited and purged abundantly, but by the hypodermic use of the aromatic spirits of ammonia the heart was kept going, and all ultimately recovered. There are cases reported in which vomiting and purging are slight, or wholly absent, and in which death apparently occurs from the effects of the poison upon the brain. In former times, when preparations of antimony were more frequently employed, chronic cases of poisoning were not unknown. Indeed, one can be fatally poisoned by the administration in broken doses of a quantity of this substance, which, when administered in a single dose, would have no other effect than that of inducing violent vomiting and purging.

The symptoms usually come on immediately after the administration of the poison, and a child has been known to die within an hour from the effects of three-quarters of a grain of tartar emetic. In another case where a young adult had swallowed an unknown quantity death occurred in seven hours, and was preceded by severe vomiting and purging. In a third case death resulted in ten hours from 60 grains of tartar emetic taken by a robust man of about 30 years of age. Immediately after swallowing the

poison vomiting and purging began, but a few hours later these ceased, the patient became insensible, fell into coma, and this deepened into death. Tartar emetic may be absorbed through the unbroken skin, and when applied to the surface it is likely to produce pustules. It is more readily taken up from abraded surfaces and wounds, and may in this way cause death. In a case reported by Kayser brownish-red cotton hose caused marked eczema, and 85 mg. of soluble antimony compound was obtained from each square centimeter of the hose. In a similar case reported by Smeltner the hose contained 177 mg. of soluble antimony compound per sq. cm.

Poisonous Dose.—A half grain of tartar emetic may produce violent symptoms in an adult, and a slightly larger quantity may prove fatal to children. It is usually stated that the smallest dose fatal to adults is about two grains. However, recovery may occur after very large doses, on account of the fact that the greater part of the poison is expelled by the vomiting and purging. Death may occur after many weeks or months from ulceration of the stomach and intestine.

Treatment.—There is no known chemical antidote for tartar emetic, and the physician called to treat a case of poisoning with this substance should immediately and thoroughly wash out the stomach and bowels. With a stomach tube the poison may be removed more thoroughly and with less exhaustion to the patient than can be done by vomiting. Therefore it matters not how frequently and constantly retching and vomiting may be going on, the physician should, if possible, immediately introduce the stomach tube, and thoroughly wash out this organ. At the same time the large intestine should be thoroughly flushed with water. After the stomach has been cleansed demulcent drinks, such as barley water, or strained oatmeal gruel, may be administered with benefit, inasmuch as they tend to allay the irritation caused by the local action of the poison. Much stress has been placed upon the use of astringent infusions, such as green tea, oak bark, etc., and it is possible that these may be of service, not on account of any combination with antimony, but from the local effects upon the inflamed tissue. However, it should be plainly understood that no reliance can be placed in any antidotal action of these substances. After the poison has been removed the administration of opiates may be resorted to for the purpose of allaying the irritation.

Post-mortem Appearances.—As has already been stated, the post-mortem appearances after poisoning from antimony differ from those induced by arsenic largely in the more destructive local changes produced by the former. Especially are these differences observable in the local action of the poison on the mucous membrane of the mouth, fauces, and esophagus. Where death has been delayed for some days the body may be covered with a pustular eruption, which, however, is not characteristic of this poison.

Mercury

Occurrence.—While metallic mercury is sometimes found free in nature it is generally prepared by heating the red sulphid, which is the most important mercurial mineral, and is known as cinnabar. The preparations most largely used in medicine are mercurous chlorid and mercuric chlorid. The extensive employment of mercuric chlorid, known also as corrosive sublimate, as a disinfectant has given great opportunity for accidental poisoning. Metallic mercury, used in filling thermometers and barometers, and in making mirrors, is so slightly poisonous that harm is not likely to come from it. It is usually stated that metallic mercury is wholly devoid of poisonous properties, and instances are known in which it has been swallowed in large amounts and has simply passed through the alimentary canal without being absorbed, and consequently without doing any permanent injury. Dr. Cox, of South Hadley, Mass., has presented the Medical Museum of the University of Michigan with a bottle containing three ounces of mercury, and accompanied by the following explanatory note: "Mount Holyoke College extends its campus quite around the ancient cemetery of the town, which dates from the days of the Revolution. In 1905 it became necessary to exhume 500 of the bodies interred therein to make ready for the 'Gaylord Memorial Library,' donated to the town. In two of the graves was found a quantity of 'quicksilver,' the old-fashioned remedy for 'stoppage,' grievously known to latter day medics as 'appendicitis.' The last desperate act in the drama, and seemingly the worst and most barbarous one that could possibly be devised, was to administer a double teaspoonful of 'quicksilver,' and if it successfully navigated and gravitated the St. Gothard of the patient the 'stoppage' was said to be overcome, and the patient, therefore, likely to recover. The accompanying specimen was recovered from the grave of a prominent citizen, whose mortal thermometer went down in 1836, at the age of 46. He and the mercury slept amicably in the grave for 69 years. Curiously enough the physician who administered the 'searchlight' was found, well wrapped in the arms of old Morpheus, sleeping peacefully by the side of his patient. The doctor never took any of his own 'quicksilver,' and so resisted the calomel, bloodletting, and stabs of Time's devastating lancet until his final 'stoppage,' which did not come until his 85th year, when he, too, passed on to the Great Forever."

When given in a finely divided state it has been known to cause death in at least two instances, and the difference in the poisonous properties of the mercurous and mercuric preparations is one of degree rather than of kind. The vapor of metallic mercury is highly toxic, and chronic poisoning is frequently observed among workers engaged in smelting ores contaminated with mercury, and those engaged in subliming this element in the preparation of certain manufactured articles. Faucher (18) reports a

case of mercurial poisoning resulting from sleeping in the upper part of an unventilated shooting gallery, in which from 3,000 to 5,000 shots were fired daily. The ethyl compounds of mercury are highly poisonous, and two chemists have lost their lives in experimenting with them.

Properties.—Calomel or mercurous chlorid is a heavy, white, insoluble powder, which, in single doses, is not believed to be poisonous, especially when given by the mouth. Runelberg (63) reports a fatal issue from the hypodermic administration of three doses of calomel, of one and one half grains each, given in the course of four weeks. Chronic poisoning with calomel occurred occasionally in former generations when this drug was given so frequently and continuously, but is now rarely met with.

Corrosive sublimate, or mercuric chlorid, is a crystalline body, usually in needles, though occasionally in octahedra, and more rarely in plates. It is soluble in fifteen parts of cold, and three parts of hot water, more soluble in the presence of the alkaline chlorids, and freely soluble in alcohol and ether. It has a biting, metallic taste, and combines with proteins with great avidity. The protiodid, blue mass, and blue ointment are largely used in the treatment of syphilis, and cases of slight chronic poisoning with these preparations are occasionally seen, but never in medicolegal investigations.

Poisonous Action.—Mercuric chlorid owes its corrosive action to the avidity with which it combines with proteins, and all mercury compounds, so far as they are absorbed, enter the blood in the form of an albuminate. This is true even of the metal itself. When absorbed from a mucous membrane, or through the unbroken skin, albuminous compounds are formed. It must not be supposed, however, that the poisonous action of mercury is dependent upon the formation of protein compounds, or that saturation with albumin renders mercury inert. The albuminate itself is poisonous, and may induce all the typical mercurial symptoms and death.

In acute mercurial poisoning, which, in a large majority of cases, is caused by corrosive sublimate, there is a burning sensation in the mouth and throat, accompanied by constriction, and due to the local action of the poison. When taken in concentrated solution the mucous membrane of the mouth may look as though it had been blistered. Soon after swallowing the poison there is pain in the stomach, and this usually is followed by severe vomiting. The ejected material at first consists of any food that may be in the stomach, and, later, of mucus, frequently stained with blood. The vomiting is soon followed by purging, and there may be marked hemorrhages from the bowels, as well as from the stomach. Usually these symptoms are followed by evidences of collapse, the pulse becomes feeble and rapid, the surface is bathed with a cold, clammy sweat, breathing is labored, thirst is intense, and in some instances there are violent cramps, especially in the extremities. Death may result quietly as a sequence of coma, or it may be preceded by convulsions, which continue one or more

days. The urine is often scanty, and may be entirely suppressed. It sometimes contains blood, albumin, and casts. Christianson points out the following distinctions in the symptoms produced by arsenic and mercury: (1) The symptoms induced by the latter generally come on much more rapidly, the irritation of the throat being recognized during the act of swallowing, and the stomach instantly endeavors to expel its contents. (2) The metallic taste of the mercury is plainly recognized. (3) The sensation of irritation along the throat is much more severe in mercurial poisoning, and (4) the vomited and purged material is more frequently mixed with blood. However, the symptoms induced by corrosive sublimate are subject to wide variations, depending upon the amount taken and the condition of the stomach, especially with reference to food content, and cases of recovery after swallowing relatively large quantities have been observed. The writer knows of a case in which a man swallowed one of the 7½-grain tablets used for disinfecting purposes. He did not vomit, but purged most violently for some hours, and otherwise was not affected.

Slight chronic mercurial poisoning, which is now rarely observed and is generally due to the continued administration of some of the milder preparations of mercury, is accompanied by salivation, sore gums, and in severe cases necrosis of the bones of the jaw. The severer forms of chronic mercurialism are subject to great variations. Frequently there is slight elevation of temperature, accompanied by chills, rapid pulse, and severe headache, with colicky pains and diarrhea. Skin eruptions may be marked. Mercurial stomatitis is accompanied by marked fetor, tendency to hemorrhage, irregular respiration, and tremor. Rheumatic pains, arthralgia, and epileptic-like seizures are sometimes observed.

Treatment.—The first thing to do in treating a case of acute mercurial poisoning is to administer large quantities of some albuminous substance, such as the white of egg. It should be understood that the advantage derived from this treatment is not due to the formation of an inert compound with the mercury. The white of egg, or other albuminous substance, saves the tissues of the stomach and other organs by furnishing a protein with which the mercury can combine. In other words, the object of the administration of the white of egg is to rob the mercurial compound of its corrosive action. The albuminate of mercury which is formed is not an inert body, and consequently it should not be allowed to remain in the stomach, but as soon as the corrosive action of the poison has been destroyed by the administration of abundant quantities of white of egg, or other albuminous substance, the stomach tube should be used, and this organ thoroughly washed. The statements made in some of our best textbooks on this subject are misleading, and if followed the result would be disastrous. It is frequently stated that with albumin mercury forms an insoluble and inert compound. It should be plainly understood that this is not true. Every particle of mercury that is absorbed into the system, either when

administered therapeutically or given in toxic doses, is converted into the albuminate before it is absorbed, and the albuminate of mercury is a highly poisonous body, but it is not corrosive in its action, because, as stated already, the corrosive action of certain mercurial compounds is due to the avidity with which they combine with proteins.

Mercurial stomatitis is best treated with a wash consisting of a dilute solution of potassium chlorate. It should be remembered, however, that potassium chlorate itself is quite toxic, and no large quantity of it should be swallowed. Astringent washes containing alum or tannic acid may also be employed, and hypodermic injections of atropin may be resorted to to lessen the flow of saliva.

Fatal Dose.—Cases of fatal poisoning have resulted from the administration of three grains of corrosive sublimate, and a much smaller amount may cause marked gastrointestinal irritation. However, owing to the speedy vomiting and purging which are likely to promptly follow the introduction of this poison into the stomach, recovery from relatively large quantities is, as has already been stated, not unknown.

External Application.—Strong preparations of mercury when applied to the unbroken skin are likely to cause serious results, and may lead to death. In these cases the symptoms resemble very closely those that are induced by administration by the mouth. The frequent employment, within recent years, of bichlorid dressings in surgical cases has shown that even very dilute preparations are not altogether free from harm when applied to wounds. Salivation, diarrhea, vomiting, and more or less marked suppression of urine have been observed in such cases. Bichlorid solutions have also been extensively used in obstetrical practice for vaginal and intrauterine washes, and several cases of poisoning have resulted therefrom. It is now generally understood that if bichlorid is used at all for irrigation purposes the solution must be very dilute, 1 to 40,000 or 50,000, and that the retention of even this dilute solution must not be permitted. It is certainly better and safer to resort to other germicides when any cavity or wound is to be irrigated.

Fatal Period.—Death may occur within thirty minutes, and it may be delayed for several days, but usually it happens within from twelve to fourteen hours. In subacute poisoning with corrosive sublimate the violent pains of the acute gastroenteritis, due to the corrosive action of the poison, abate on the second day, and the victim seems much better, but later the effects of the absorbed poison manifest themselves, and may lead to death. The general symptoms consist of mercurial stomatitis and glossitis, with the formation of ulcers in the mouth, salivation, accompanied with fetid breath, bloody stools, albuminuria, hematuria, and finally anuria. In nonfatal cases the condition of the alimentary canal, especially of the mouth and salivary glands, may become chronic, and in some instances pustular eruptions appear on the skin.

Post-mortem Findings.—In acute mercurial poisoning, whatever may have been the method of administration, there will be a brownish or black coloration of the gums, and marked inflammation, with ecchymoses in the mucous membrane of the alimentary canal. It is true that when death results a few minutes after the administration of a large dose histological changes are not prominent. When a large quantity of corrosive sublimate is swallowed the effects observed on post-mortem examination resemble those induced by mineral acids. There may be marked inflammation of the mucous membrane of the mouth, pharynx, and larynx, together with edema of the glottis. In fact, in some instances, death from mercurial poisoning, especially those cases which terminate speedily, is due to edema of the glottis. The erosions in the stomach and intestines may be extensive and deep, even to perforation. Ulceration of the ilium and a diphtheritic condition of the large intestine, with or without perforation, have been observed. Frequently the mucous membrane from the mouth to the pylorus is found diffusely colored. Ludwig reports a case in which the mucous membrane of the esophagus and stomach appeared as if it had been cooked. The bronchial tubes may be highly inflamed, and ecchymoses on the endocardium may be found, while degeneration of the muscle of the heart has been seen even in cases which terminated fatally within two or three days. The marrow of the bones may be highly injected. Ulcers have been found on the gums, and the kidneys and liver show lesions which will be described later. According to Virchow the anatomical changes in the large intestine cannot be distinguished histologically from acute dysentery. Chemically, mercury can be detected in the tissues. However, the intestine is not invariably seriously involved, as cases have been reported by competent observers in which no changes, or those of only slight degree, could be detected. According to Kaufmann, involvement of the intestinal walls depends upon the formation of thrombi in the capillaries, with consequent necrosis, while the diphtheritic condition is ascribed to the action of bacteria. In acute poisoning from administration by the mouth peritonitis with a bloody serous exudate may occur.

The changes in the kidneys are most interesting. If a section of this organ be placed under the microscope and treated with dilute sulphuric acid effervescence takes place, and the formation of crystals of gypsum may be seen. This is due to the fact that in mercurial poisoning calcification occurs in the renal epithelium. In cases terminating within a few hours the kidneys are hyperemic, and frequently show hemorrhagic spots. When the poisoning is less rapid the condition resembles that of acute parenchymatous nephritis. On microscopic examination there will be found cloudy swelling and necrosis of the cortical tubules. Fatty changes may or may not exist. Hyalin or granular casts may be found in the tubules, and the interstitial tissue may be infiltrated with small cells. Deposits of lime are found in the tubules, most abundantly in the convoluted ones. The ques-

tion has arisen whether or not this calcification of the kidney can be regarded as pathognomonic of mercurial poisoning. Weichselbaum states that it cannot be so considered, because it is seen in poisoning with certain other substances, as manganese, bismuth subnitrate, glycerin, etc., but he adds that the finding of abundant chalky deposits in the convoluted or straight tubules of the cortex should be taken as a strong suggestion of mercurial poisoning. The cause of these deposits is an interesting question. The old theory that the lime deposited in the tubules is withdrawn from the bones has been shown to be erroneous. Kaufmann offers his theory of thrombosis in explanation, but it is more rational to explain the calcification upon the supposition that the epithelium, injured by the mercury, is no longer able to eliminate the lime salts. This, with the diminished secretion of urine, which may lead to anuria, is probably sufficient cause for the formation of deposits. In this connection it is interesting to state that the researches of E. Ludwig have shown that the places of predilection for the deposit of mercury are the kidneys, liver, and walls of the large intestine, in the order named.

Muscular tremor is one of the common manifestations of mercurial poisoning. Paralysis of the upper extremities may occur, and may be accompanied by atrophy. A microscopical examination of the nerves shows cloudiness and granulation of the neurilemma, without alteration of the axis cylinder. The malar necrosis resembles that caused by phosphorus. There is much difference of opinion concerning the effects of chronic mercurialism on the bones. Since so many of the individuals in whom these lesions have been studied were syphilitic it is difficult to decide to what extent the changes in the bones should be attributed to this disease, or to the effect of the mercury.

Copper

Occurrence.—Copper is one of the most widely distributed metals. In certain localities large masses of native copper are found, although the great copper mines consist for the most part of ores such as carbonate, oxid, and sulphid. While there are relatively few localities in which copper ore exists in sufficient quantity to make its extraction commercially successful this metal is found in traces in nearly all soils. Apparently there is no copper ore which interferes with the growth of plants, and the metal is taken up in greater or less quantity by most of the vegetables which furnish food for man. Each kilogram of wheat contains from four to ten milligrams of copper, and rye, barley, oats, rice, corn, and buckwheat are equally rich in this mineral constituent. The exact amount found in these cereals varies with the copper content of the soil in which they are grown. However, analyses made in different countries by different men show that the variation is not so great as one would suppose. On account of its con-

stant presence in cereals copper may be looked upon as a normal constituent of bread, in which the amount is usually less than 5 milligrams per kilo. Potatoes contain from 1.5 to 3 milligrams per kilo, and this element is found in practically the same amount in peas, beans, and cucumbers, and in such fruits as cherries, pears, apples, etc. It also exists in grapes, yeast, and wine. In many of the lower animals copper is a widely distributed element, and in some it apparently serves a physiological purpose. In the crustacea, arachnoids, gastropods, and cephalopods a copper-containing protein known as hemocyanin apparently serves the purpose accomplished by hemoglobin in the blood of mammals. According to Bizio, the ash of certain snails contains as much as 2.4 per cent. of the oxid of copper, and Cousent, Ferrand, Lehmann, and others have shown that oysters are especially rich in this metal. Cousent obtained from twenty-five oysters secured on the Falmouth banks 216 milligrams of copper. As early as 1830 Sarzeau reported the presence of copper in the blood and flesh of the ox, and this statement has been confirmed by Cheveraul, Orfila, Devergie, and others. Orfila was the first to announce that copper is a constituent of the normal tissue of man. This statement was at first denied, but subsequent investigation has shown it to be true. Lehmann has collected a large number of analyses made by different persons, and has shown that copper is found in the tissues of the higher animals, including man. The amount varies with the organ examined, and is largest in the liver as a rule. Only rarely is it found to be altogether absent. The amount found in the liver of man varies from 1.5 to 15 milligrams per kilo. The liver of the ox may contain as much as 50 milligrams per kilo. Traces of copper are frequently found in drinking water, and especially in mineral waters. Beer, wine, and brandy almost invariably contain copper. Vinegar often contains traces of this element, and when kept in copper utensils the amount becomes relatively large, and in one liter there has been found as much as 140 milligrams. Fatty acids dissolve copper, and consequently butter brought in contact with copper receptacles becomes contaminated with this metal. Experiments by Lehmann show that both salted and unsalted butter dissolve copper. The green coloration of some cheese, notably those of Italian make, is in part due to the presence of salts of copper. It should be understood, however, that the green color of most old cheese is largely due to the presence of molds. Much has been said about the use of copper in coloring canned articles of food, especially peas and beans. The usual method of doing this is to place peas in water to which a definite amount of copper sulphate is added, allowing the peas to stand in this copper solution for a definite period of time, and then removing them. For many years the French government forbade the coloring of peas and other vegetables with copper, but in 1889 a commission was appointed to investigate the matter, and as a result of the studies of this commission the law on this subject was repealed. It has been found that when

peas which have not been colored with copper are sterilized in the process of canning they acquire a brownish, sometimes a yellowish, color, and the copper is added to prevent this change. According to Tschirch the coloring matter formed in the pea is a copper chlorophyl compound. This author states that when uncolored peas are heated in the process of canning the brown coloration is due to phyllocyaninic acid, and that when copper is added the brilliant green compound, phyllocyaninate of copper, is formed, and this compound is not altered by the heat used in sterilizing. When an excess of copper is added, or the peas are left for too long a time in the copper solution, the proteins combine with copper, forming a bluish compound. For this reason the manufacturer of canned peas endeavors to avoid an excess of copper, inasmuch as he finds that such an excess renders his product less pleasing to the eye. While the amount of copper in colored peas varies, it is as a rule less than 100 milligrams per kilo. It will be seen from this that one obtains more copper in a dozen oysters than he would in eating more than two pounds of peas. Lehmann claims that from the most remote historical times down to the middle of the eighteenth century copper cooking utensils were largely employed, and, so far as we know, serious harm seldom came from them. It is fortunate, however, that iron has taken the place of copper for these domestic purposes, and it must be admitted that without proper attention to cleanliness verdigris might be formed in sufficient quantity, especially when acid foods are allowed to stand in unclean copper vessels, to seriously poison man. We have refrained, in discussing the occurrence of copper, from giving references to literature, because this whole subject has been carefully and exhaustively treated by Lehmann, to whose article we refer those desirous of looking up the literature (42).

Poisonous Action.—Copper sulphate, or blue vitriol, and copper subacetate, or verdigris, are the two salts of this metal most frequently employed. The former is sometimes used as a disinfectant, for which purpose it is of but little value, and frequently finds its way into the household. Cases of accidental poisoning occasionally occur, and suicides sometimes resort to one or the other of these preparations. However, all the soluble ores of copper are poisonous when administered in sufficient quantity. In acute poisoning the mucous membrane of the alimentary canal throughout its entire length is inflamed and changed to a greater or less degree. Ecchymoses may be found anywhere along the tract, and ulceration may occur in the stomach, small or large intestine, and may proceed to perforation. Patches of green or bluish coloration are occasionally observed. The hemoglobin of the blood is more or less broken down, with the formation of an excess of bile pigment, leading to marked icterus, which, according to Tidy, is of special value in the diagnosis of poisoning by copper, inasmuch as it is not observed after poisoning with either arsenic or mercury. Unless death occurs within twenty-four hours fatty changes in the liver

and kidney may be found, and the latter organ may also show signs of acute parenchymatous degeneration. The metal, albumin, casts, blood, and bile pigments may be found in the urine.

Fatal Dose.—Inasmuch as the salts of copper are markedly emetic, recoveries from very large doses have been reported, and it is quite impossible to give exactly the amount likely to prove fatal. Formerly the acetate of copper was largely used as an emetic in cases of so-called croup, and in the course of a few days two or three more drachms of this substance have been administered without other effect than the nausea and vomiting thus intentionally induced. The minimum fatal dose for an adult of either one of these salts is probably about half an ounce.

Symptoms.—Fifteen grains or more of either the sulphate or acetate causes nausea and vomiting, which become more marked under the influence of larger quantities. In general we may say that in acute poisoning with copper the symptoms are those of gastrointestinal irritation, and are not distinguishable from those due to other irritant poisons. In some cases the nervous system seems to be profoundly affected, and severe convulsions, which may or may not be followed by coma, precede death. In chronic poisoning with this metal there are a metallic taste, colicky pains, diarrhea with bloody stools, scanty urine, dry parched skin, occasionally jaundice, and, in severe cases, cramps and convulsions. Chronic poisoning with copper, sometimes seen in workers in brass, is characterized by emaciation, anemia, tremor of the tongue and hands, myalgia, and neuralgia. A dark-green line may often be detected on the gums, especially when the teeth are not clean.

Treatment.—White of egg, milk, or some other albuminous substance should be administered in order to destroy the corrosive action, and the stomach tube should be used immediately. In fact, the stomach might be washed out before albuminous substances are administered, but in this case the washing should be repeated after the administration of milk or egg. The stomach should be distended with water and thoroughly cleansed. Fortunately, the salts of copper are fairly soluble in water, and there is little difficulty as a rule in completely removing the poison. At the same time the large intestine should be flushed. Chemically, ferrocyanid of potash may be administered, inasmuch as this forms an insoluble and practically inert compound with copper. However, reliance should not be placed on the chemical antidote to the extent of neglecting the use of the stomach and rectal tubes.

Post-mortem Appearances.—The mucous membrane of the alimentary canal, usually from the mouth through the intestines, will show the effects of an irritant, inasmuch as it will be inflamed, and possibly ulcerated. A greenish or bluish tint may be perceptible and the presence of copper in these colored spots may be detected by the addition of ammonia, when the color becomes deep blue. Large ulcerations have been found in the

rectum, and rarely the intestine is found to be perforated. The microscopical examination of the mucous membrane of the stomach, after poisoning with copper, shows superficial necrotic changes. The nuclei of the epithelial cells remain uncolored; there is marked dilatation of the veins of the mucosa and submucosa, and these are filled with blood corpuscles, some of which retain their form, while others consist only of cellular débris. Usually there are extensive blood extravasations in the submucosa. A clean knife blade immersed in the greenish-blue contents of the stomach, after the addition of dilute hydrochloric acid, is soon well coated with metallic copper.

TIN

Occurrence.—The most important tin ore is cassiterite, which is an impure oxid. This ore is freed from arsenic and sulphur by roasting, after which it is washed and then fused with coal and lime. Tin pyrites are sometimes used for the preparation of the metal. Tin utensils consist of iron, coated with tin. Tin is more or less soluble in dilute acids, both inorganic and organic.

Symptoms.—Poisoning with tin is rare, but not wholly unknown. Most of the soluble salts are gastrointestinal irritants, causing nausea, vomiting, purging, and collapse. Most cases of poisoning from tinned foods are due to imperfect sterilization and fermentation changes in the contents of the can. However, there are recorded a few instances in which the harmful substance has undoubtedly been a soluble salt of tin. This is apparently true of the cases reported by Luff and Metcalf (49), which were due to the eating of canned cherries, in each fluid ounce of which there was found 3.2 grains of tin malate. It has been shown by Ungar and Bodlander (72) that the subcutaneous injection of the nonirritating salts causes cell injury, and death in the lower animals.

Treatment.—The stomach should be washed and demulcent drinks administered.

LEAD

Occurrence.—In nature lead occurs most abundantly as a sulphid, known as galena, although some large lumps of native lead have been found in several localities in Missouri. This ore is frequently found in deposits containing more valuable minerals, and its separation is not only expensive, but to some extent dangerous, inasmuch as lead poisoning is not infrequently observed among those engaged in smelting silver ores. The soluble form of lead which is most frequently employed in commerce is the acetate, ordinarily known as sugar of lead, while the carbonate is largely used in paints, more in former times than at present.

Poisonous Action.—Lead combines readily with albumin, and some of the lesions found in the alimentary canal after poisoning with this substance are due in part to this action; but that lead is a poison merely on account of the readiness with which it forms a compound with albumin is not true, because the albuminate of lead and other noncorrosive compounds of this metal are quite as poisonous as the inorganic salts. Some preparations of lead are supposed to be abortefacients, and the supposition is well grounded if the life of the mother is also to be sacrificed. Most cases of lead poisoning are either industrial or accidental. When lead paints were largely employed both acute and chronic plumbism was by no means rare. Moreover, lead colic and drop wrist were frequently seen among those engaged in smelting lead ores. Next to the above came instances of poisoning with sugar of lead, lead foil, and other preparations. For homicidal purposes the salts of lead are seldom employed; according to Hugounenq (29) only twelve cases were officially known during the latter half of the past century.

Poisonous Dose.—According to Kobert the minimum fatal dose of the three preparations of lead most generally employed are as follows: lead acetate, 20 g., white lead, 25 g., and sugar of lead, 50 g.

Symptoms.—Acute lead poisoning, practically always due to acetate, is rare. However, the writer has seen three or four cases in which this salt of lead has accidentally caused serious results. The symptoms are those of gastrointestinal irritation, vomiting and retching being prominent. The bowels are generally obstinately constipated. This is due to the contraction of the walls of the large intestine. At first the abdomen is retracted, and is not painful on pressure; indeed, the colicky pains which are almost constant in this form of lead poisoning are frequently relieved during the earlier stages by marked pressure over this region. Some years ago the writer was called to treat a case of acute lead poisoning, which was caused by eating tomatoes cooked in a vessel the bottom of which had been burned out and had been mended by lead solder. The victim, an elderly man who lived by himself and prepared his own food, showed the characteristic blue gums very distinctly, and complained bitterly and constantly of severe colicky pains. The abdomen was markedly retracted; in fact, it might have been said to have been dished. Every attempt to evacuate his bowels either by the administration of saline purgatives or by the use of the rectal tube was without avail. At the expiration of 48 hours the man died, and it was found that 14 inches of the descending colon just above the sigmoid flexure was so tightly constricted that even air could not be forced through it. In some instances the vomiting is severe and protracted, and the vomited material may be stained with blood. The pulse becomes frequent and irregular, the breathing shallow, and coma may precede collapse and death. In acute lead poisoning, if fatal, death usually occurs in two or three days, otherwise there is partial

recovery, and the condition becomes chronic. In rare instances the chromate of lead is used for coloring foods, and cases of acute poisoning have resulted in this way, although the affection is more likely to be chronic. The cases in Philadelphia so well studied by Stewart (68), in which "Chrome Yellow" (lead chromate) was used for coloring buns, are especially interesting. Some 64 cases or more were found, and nearly every symptom of lead poisoning seen in the different ones. The blue line was observed in 89 per cent., colic in 76, headache in 73, and convulsions in 17 per cent. Inasmuch as acute lead poisoning may be accompanied by marked elevation of temperature, it may, especially in the later stages, be mistaken for peritonitis. One such case has come under the writer's observation. In the neighborhood of lead smelters domestic animals are frequently affected with this poison. In these the nervous symptoms are often more marked than in man. Convulsions and tremors are frequently observed, and if the abdomen is opened the intestines are found tightly constricted, and this condition is relieved by the administration of large doses of atropia. It is stated that children may be poisoned by the milk of "leaded" cows, but if this be true at all it certainly is of rare occurrence.

Chronic lead poisoning is much more common than the acute form, but is not so frequently met with now as formerly, inasmuch as lead paint has been largely supplanted by zinc compounds. However, chronic lead poisoning occurs not only among workers in white lead, but also in smelters engaged in reducing lead ores; also from the use of lead as a cosmetic, and the writer has known of two instances in which chronic lead poisoning resulted from the drinking of bottled beer from a brewery in which it was the custom to cleanse the bottles with shot. Chronic lead poisoning may also result from the inhalation of the finely divided metal, and it is occasionally known, though rarely, to result from drinking water conducted through leaden pipes. Lead foil, used in packing tobacco, cheese, and other articles, is also a source of chronic poisoning. It is stated that occasionally thread contains enough lead to poison the one who is accustomed to moisten it in order to pass it through the eye of the needle. Roque and Linossier (62) report six cases of lead poisoning among women engaged in spinning cotton colored with lead chromate. Usually the first symptom of chronic lead poisoning is colic, which, when occurring among painters, smelters, or others engaged in the use of lead compounds, should always awaken suspicion, and should lead to the chemical examination of the urine. Lead colic in chronic cases is usually accompanied by a sweetish metallic taste, and the deposition of a characteristic bluish line along the base of the teeth. This is more marked when the teeth are not kept clean, and is due to the formation of the sulphid. Drop wrist is a fairly characteristic symptom of lead poisoning. It is due to paralysis of the extensors of the fingers and hand. There may be contractures of the flexed

fingers. Frequently there is a more or less local anesthesia, and disturbance of vision, such as amblyopia and amaurosis, are frequently met with. Exophthalmia is seen more rarely. In lead encephalopathy there may be most grave disturbances in the central nervous system, which manifest themselves by choreic movements, epileptic or cataleptic seizures, and sometimes by wild delirium. These seizures are likely to be periodic, and during the intervals the patient may be quite free from any nervous manifestation of disease.

Fatal Dose.—The minimum fatal dose of the acetate of lead is not known. An ounce has been swallowed at one time without serious result, while half this quantity has been known to induce alarming symptoms. A quantity that would have but little effect if taken at one time may induce serious chronic poisoning if taken in small portions daily.

Treatment.—The soluble sulphates, such as magnesium, may be administered with benefit in acute lead poisoning, inasmuch as lead sulphate is practically insoluble. In chronic poisoning magnesium sulphate may be given as a cathartic, but otherwise it can be of no great value. The administration of potassium iodid has been supposed to assist in the removal and elimination of lead deposited in the tissues. Atropin is supposed to be of value in the relief of the intestinal constriction frequently seen in chronic lead poisoning.

Post-mortem Findings.—In acute lead poisoning gastritis is generally more or less marked, and there may be ulceration. The mucous membrane of the intestines is shriveled, anemic, and frequently stained grayish brown by the sulphid of lead. In animals experimentally poisoned serous effusions under the membranes of the brain and cord have been observed. Coen found inflammatory infiltrations in the lungs, liver, and kidneys, with cloudy swelling and vacuolization in the epithelium of the stomach, intestines, pancreas, kidney, adrenals, and liver, but no evidences of fatty changes.

Chronic lead poisoning furnishes the pathologist with abundant material for study, inasmuch as the lesions are decided in degree and extensive in area. Disturbances in the alimentary canal occur, whatever may have been the avenue of administration. Coloration of the gums is one of the signs of chronic saturnism first looked for by the physician. Massazza observed it in dogs three days after the administration of the poison was begun, but generally it appears much later. Both the gums and teeth are often stained, and sometimes the insides of the lips and cheeks show bluish patches. Ulceration of the stomach and upper intestine is occasionally found. The peptic glands undergo fatty degeneration, and may be obliterated in certain areas. The mucosa is thickened on account of proliferation in its connective tissue. The solitary and agminated glands suffer fatty degeneration or atrophy, and similar changes may be detected in the muscular walls of the stomach and intestine. There may

be contractions in the connective tissue of the walls of the alimentary canal, leading to abnormalities of form and position.

It is generally believed that lead is eliminated to some extent by the skin. Cases of chronic poisoning have been reported in which the epidermis has been darkened on the application of a dilute solution of sulphid of sodium, or after bathing in water impregnated with hydrogen sulphid gas. However, perspiration collected after the administration of pilocarpin in these cases has been found to be free from lead. Kobert suggests that the poison may be contained in the epidermis in an insoluble form. Lesions of the skin are not constant in this affection, but may occur; the most common form is a pustular erythema. The existence of an icterus saturninus has been both affirmed and denied by good clinicians, which shows that it may occur, but is not constant. In long-continued saturnism the subcutaneous fat disappears, the skin becomes wrinkled, dry, and brown, giving the appearance of old age. The local anesthesia already referred to is due to the action of the poison on peripheral sensory nerves, and is transitory. The number of red corpuscles and the amount of hemoglobin are diminished. According to Grawitz, the red corpuscles in lead poisoning often contain basophilic granules, staining with methylene blue. The disturbances of vision often occurring in chronic saturnism are probably secondary to the effects of the poison on the kidneys. Stood divides them into two classes: The first he considers a neuritis due specifically to the action of lead, and he states that it may occur without the coexistence of albuminuria. The second he regards as a retinitis, such as may accompany a contracted kidney due to other causes. Between and connecting these is hydrops of the sheath of the optic nerve, which may be a consequence either of nephritis, with hypertrophy of the left ventricle, or of peripheral retrobulbar neuritis. The neuritis generally begins with inflammatory pneumonia, easily recognizable with the ophthalmoscope; but it is often impossible to determine exactly what part of the nerve is most seriously affected. According to Oeller, hyalin deposits in the vessels of the choroid and retina may be found in some cases of lead poisoning.

The minute anatomy of the contracted kidney of chronic lead poisoning has been studied by numerous clinicians and pathologists, but their findings have led to diverse views. In brief, it may be stated that some contend that the lesions begin in the blood vessels. The arteritis, they say, leads to contraction here and there, and to occlusion of the lumen of the blood vessels, while the parenchyma secondarily becomes atrophied and the interstitial connective tissue proliferates more or less. Others hold that lead first injures the secreting elements, and that the affection of the blood vessels is secondary, and in no wise characteristic. Guyler believes that the primary and most important histological changes are found in the blood vessels and begin in the endarteritis, which leads to obliteration of the capillaries. The process differs from an ordinary arteriosclerosis

in the disappearance of muscle cells, with thickening of the middle layer by the growth of fibrous tissue. The endothelium proliferates and contracts the lumen. The walls thicken by the deposition of the granular material, which later becomes homogeneous. Finally complete occlusion results, and the capillaries involved are converted into glistening, compact, homogeneous tissue. He designates the process as "vasculitis capillaris obliterans." The sequelæ and the alterations in the kidney are identical with those which follow contracted kidney from other causes. In chronic lead poisoning a typical form of atrophic cirrhosis of the liver may be induced.

Lead arthralgia is not accompanied by any constant or characteristic lesions. In lead gout uric acid may be deposited in the contracted kidneys and in various joints. Lead paralysis, although common in chronic saturnism, is not constant. The musculospiral is the first and often the only nerve involved. So constant is this that paralysis of this nerve or its branches is generally regarded as due to lead even when inquiry fails to reveal the manner in which the poison has been introduced. "Drop wrist" may result from the external application of preparations containing lead, as well as when the poison is taken by the mouth. Atrophy of the muscles usually follows paralysis, but in some instances may precede it. Rarely the deltoid or the biceps is more seriously affected than the muscles of the hand and wrist, and the peroneal muscles are sometimes involved. General paralysis as a result of lead poisoning has been reported, and paralysis of one or both vocal cords is said to be a typical symptom of lead poisoning in horses, while paralysis of the adductors of the larynx has been observed in man. Atypical paralyses are likely to result from the combined action of two or more poisons, as lead and alcohol, and lead and syphilis. Examination of the parts involved in lead paralysis shows changes in the muscles, blood vessels, and nerves. The alterations in the muscles may be macroscopic. They are much wasted and pale or yellowish. Microscopically certain fibers will be found to be altered, while others are quite normal. The diseased fibers are shrunken and sometimes show an enormous proliferation of nuclei. The position of a fiber may be indicated only by the presence of granular débris and clusters of nuclei. The changes in the vessels are those of arteritis obliterans. Changes in the nerves are most evident in their peripheral terminations, but may extend backward to the trunks, and are thus seen in other forms of neuritis. It is a question whether the conditions observed in lead encephalopathy are due to the direct action of the poison on the brain cortex or result from the general arteriosclerosis and changes in the kidney. Be this as it may, the most exhaustive researches have failed to show either gross or minute lesions in the brain.

Zinc

Occurrence.—Zinc is not widely distributed in nature, and is found most abundantly as a carbonate and oxid. Metallic zinc is largely used in the manufacture of metal vessels of various kinds, but the only salts of zinc which interest the toxicologist are the sulphate and chlorid, the former being known as white vitriol.

Poisonous Action.—The sulphate of zinc is only slightly poisonous, and on account of its emetic properties recovery from large doses may occur. However, death may result from half an ounce or more. Zinc chlorid is the only actively corrosive compound of this metal, and its action is characterized by the formation of a hard, dry crust which remains in place. Blyth reports a case of a woman who died after the application of a large amount of this salt to her cancerous breast. Practically the only use made of the chlorid in medicine is due to its caustic properties, and it is not administered internally. Chronic zinc poisoning among those engaged in smelting has been frequently observed, but it is questionable how much of the ill effect is due to zinc and how much to associated metals, as lead and arsenic. Much has been said about the possibility of poisoning resulting from zinc solder used in canning foods, and from the employment of ice-cream freezers made of this metal. So far as we can ascertain statements along this line have been largely sensational, and we have failed to find any convincing evidence that any one was ever poisoned by zinc obtained from either of these sources. When a teaspoonful of ice cream causes nausea and vomiting it is the height of absurdity to think that this can be due to some soluble salt of zinc, because if there should be enough of the zinc salt present to cause these symptoms there would be no room for ice cream in the spoon. Occasionally the chlorid or sulphid of zinc is taken accidentally, or for suicidal purposes. When used with the last intention it is generally a failure. Blyth reports one death which resulted six weeks after taking six grains of the chlorid. It is barely possible that if this amount was taken in concentrated solution it might have caused local ulceration which subsequently led to infection, and this to death; otherwise we think his verdict in this case doubtful. Another instance is reported in which a man, while intoxicated, swallowed four ounces of a saturated solution of zinc chlorid. This was followed by excruciating pain in the stomach, and later by convulsions and epileptiform fits. The local irritation led to partial occlusion of the esophagus and contraction of the stomach. Gastrostomy was not performed. The patient was fed entirely by enemata, and death resulted from starvation after eleven weeks. The only case involving zinc salts in which the writer was ever consulted was a malpractice suit against an irregular physician, who, it was claimed, had used the chlorid of zinc instead of the sulphate as an eye wash. How-

ever, the justice of this claim was questioned, and at any rate only a temporary injury resulted.

Treatment.—In case of acute poisoning with a soluble salt of zinc mucilagenous drinks should be given, and the stomach tube used.

Silver

Poisonous Action.—The only preparation of silver from which poisoning may result is the nitrate. In acute poisoning with this salt its caustic action is responsible for the most prominent lesions. The nitrate of silver in strong solution, or in the form of lunar caustic, produces a more or less deep eschar. On portions of the body exposed to the light this eschar soon turns brown or black, while on the mucous membrane it may remain white. It consists of the albuminate of silver, and the change in color on exposure to light is due to reduction to metallic silver or one of the lower oxids. Post-mortem examination after acute poisoning shows only escharotic lesions in the mucous membrane.

Chronic poisoning with silver is known as argyria, and is of marked importance to the pathologist. Since the publication in 1859 of the now classic paper of Fromann on the pathological lesions of argyria much interest has been manifested in this subject. Formerly nitrate of silver had some repute in the treatment of epilepsy, and many cases of argyria resulted from its employment in this disease. In a case of ulcerative colitis treated at the hospital of the University of Michigan the colon was washed daily with a solution of silver nitrate (one dram to four pints), and well-marked argyria occurred within eight months. The subject of Fromann's studies had taken three and a half ounces of silver nitrate in pill form within about ten months. During the greater part of this time he took one six-grain pill each day. The face began to show evidence of pigmentation about two months after the treatment was begun, and the coloration gradually deepened and extended to other parts of the body. A chronic gastritis developed, accompanied by pain, which at first was intensified only on taking one of the pills, but later also by food. There was frequent vomiting, and restriction to liquid food was finally necessary. In view of the fact that nitrate of silver has been recommended by some as a curative agent in tuberculosis it is interesting to know that this patient developed tuberculosis while saturated with silver. The only parts of the skin free from pigmentation were the palms of the hands and the soles of the feet. In the brain the Pacchionian bodies were prominent; the arachnoid showed some cloudiness, and the choroid plexus was grayish blue. Pigment indurations and calcified tubercles were found in the lungs, together with cavities and miliary tubercles. The walls of the left ventricle of the heart were much thickened. The mucous membrane of the stomach was reddened and dotted with small hemorrhagic erosions, while an oval

ulcer, 7 cm. long and 5 cm. broad, occupied the posterior wall midway between the cardia and the pylorus. The floor of this ulcer was uneven, and at one spot it consisted of the pancreas, the stomach being perforated and adherent to this organ. There was a stricture of the pylorus, apparently due to hypertrophy of the muscular and submucous layers. The mucous membrane of the small intestine was thin, and the lumen constricted. The follicles were filled with black granular deposits. Under the microscope these were found to vary much in size and form, but were not crystalline. On treating a thin section containing these granules with a solution of potassium cyanid they disappeared. Similar granular deposits were found abundantly in the spleen. The liver was small, filled with blood, and its cells showed fatty changes. Granular deposits were observed in the middle of the acini, apparently surrounding the small veins. On microscopic examination of a cross section the lumen of the vessels was seen to be inclosed by black rings. Deposits of silver were abundant in the kidneys, and it is to these organs that students of argyria have subsequently given most attention. Fromann found that the pyramids were stained dark gray, the color being deepest near the papilli and becoming lighter toward the cortex. On section of the cortex the glomeruli appeared as black dots. Microscopically they were found to contain finely granular material which conformed to the shape of the vessels, and were quite distinct in the capsule. Some glomeruli were more extensively colored than others. Unchanged Malpighian bodies were found to be few. Like finely granulated material was observed deposited in the blood vessels on and between the walls of the tubules of the pyramids. Toward the papilli these deposits were most abundant, becoming less toward the cortex, but not disappearing altogether. On cross section the tubules appeared to be surrounded by a distinct black ring. The walls of the convoluted tubules showed no abnormality except fatty changes in the epithelium. These granular deposits dissolved in solutions of potassium cyanid, and became white and opaque on the addition of nitric acid, and again black on subsequent treatment with ammonium sulphid. Other investigators have confirmed the statements of Fromann, but von Kahlden finds the histological changes in the kidneys more marked than others have supposed. It might be conjectured that the individual from whom von Kahlden obtained his material suffered from coexistent disease, to which these lesions might be attributed, but he points out that the distribution of the histological changes corresponds exactly with the deposits of silver; and, moreover, he found a similar condition in a rabbit in which argyria had been induced experimentally. It is supposed by Riemer that the silver compound is reduced in the intestine, and the finely divided metal is taken up by the blood and lymph and mechanically deposited in the kidney, but Naunyn has shown that the distribution is different from that which occurs when a finely divided pigment is employed. It is claimed by Loew that in the body silver is reduced by the living cell

only, and that a more exact study of the blackened glomeruli shows that the silver is deposited in the endothelial cells surrounding the Malpighian bodies.

According to Rozahegzi, chronic poisoning with the salts of silver in the lower animals induces hyperemia of the mucous membrane of the trachea and larynx, and edema in the lungs. In some instances hepatized areas were found in the lungs. The pulmonary epithelium showed fatty changes, while the connective tissue of the walls of the alveoli evidenced proliferation. Fatty changes in the liver cells, accompanied by hyperplasia of the interlobular connective tissue, may be seen, as in both the convoluted and straight tubules of the kidney the epithelium is found to be swollen and granular, and in certain localities the detritus resulting from disintegration filled the lumen.

Borax and Boric Acid

Occurrence and Properties.—Borax, or sodium borate, and boric acid are widely distributed in nature, being found in abundant deposits in certain volcanic regions, in traces in the water of the ocean, in the crust of the earth, and in many plants. Traces are present in wine and beer naturally, coming from the grape-vine and from hops, and probably in most fruits. Boric acid is sparingly soluble in cold, more readily in hot, water. Borax is more freely soluble in both cold and hot water. It is a question whether or not these preparations should be classed among the poisons. There is only one instance in medical literature, so far as I have been able to find, in which boric acid has been given as the cause of death, and in this case, reported by Schwyzer, a man, 60 years old, took one dose of 15 grams. This was followed by colic, diarrhea, collapse, and anuria. Section showed slight irritation of the gastrointestinal mucous membrane and acute degenerative changes in the liver and kidneys. Microscopical examination showed the convoluted tubules filled with coagulated albumin and epithelial casts. In animals killed with massive doses there are marked gastroenteritis and fatty degeneration of the liver, kidneys, and heart. The only reason for introducing the boracic preparations in a work on toxicology is that they have been largely used as food preservatives, and in this connection have received much attention in medicolegal investigations.

General Statements.—Many scientific and medical men have expressed opinions concerning the effect of borax and boric acid on the animal economy. These opinions have been formed in some instances after long experience in prescribing these preparations, and in others after more or less carefully conducted experiments. The Senate of the 56th Congress appointed a committee on Food Adulteration, and the testimony taken has been published (65). From this volume we make a few abstracts. Hen-

rotin stated: "As regards the use of boric acid I am perfectly willing to state that I consider the material absolutely innocuous and able to be taken into the human economy in large and continuous and repeated doses for a great length of time without a particle of harm resulting, which comprehends about what I know, except to state that my knowledge is based upon an experience of a great many years in using boric acid and borax, both internally, for various forms of disease, and externally, using it every day of my life. I think—for my profession is almost all confined to surgery—as surgical dressings, and applications to the throat, and to the different cavities of the body. I have used borax and boric acid in, I think, nearly all the cavities of the body, used it in the large cavities, in the stomach, in the abdominal cavity, in the bowels, in the vagina, in the uterus, in the nasal passages, and in fact almost every reachable portion, and many cavities that are opened and closed afterward, and never since I have used boric acid have I seen the least deleterious effect of it in any way, shape, or manner, and the same applies to borax."

Haines testified: "Some antiseptics I regard as unquestionably harmful. Others are, when used in proper proportions, practically harmless. In this category I think we may place common salt, although criticism may be offered respecting its use; saltpeter, concerning which also severe criticism may likewise be offered, and boric acid and its various preparations; and I may say at the start that I believe that of these boric acid and its preparations are, on the whole, to be preferred to the other antiseptics mentioned for various reasons. In the first place, they produce less effect upon the articles preserved. Common salt and saltpeter impart considerable taste to meats, and therefore make them less palatable. Common salt and saltpeter affect the fiber of meats disagreeably, especially if an excess of them is used, and make them less palatable and digestible, while boric acid and its preparations have scarcely any effect, if used in small quantities, in this direction. Common salt and saltpeter have a tendency to cause the juices of the meat to exude and run away, and very much of the valuable portion of the meat is thus lost. Boric acid and its preparations produce these effects to a much less extent, and the juices of the meats are more nearly retained in their natural condition. For all these reasons I believe that boric acid and its preparations are to be preferred to common salt and saltpeter if used in moderation. The toxicity or poisonous character of these substances ought, of course, to be compared. It is true that a certain number of cases have been reported of bad effects from boric acid and its preparations, but upon looking up the records I have failed to find a single case in which these unwholesome results could not be attributed reasonably to an excessive dose, or to the disease for which the acid was employed, or to idiosyncrasies, or to impurities in the acid used. As to the first of these matters (the use of excessive doses) it is well known that common salt, when used in large quantities, is danger-

ous, and we have cases of death from excessive doses of it. Saltpeter has caused many deaths; in one publication alone I find a record of 8 to 10 deaths from it. Boric acid has caused fewer deaths than the other two substances."

Edwards stated: "It (boric acid) is the ideal preservative, superior even to common salt, because of the lack of change of the substances to which it is added for preservation."

Billings said: "It (boric acid) has come in recent years into more common use in preserving meats, especially hog products, and in preserving butter, because it was found that those things kept better with it than they did with common salt. And to my mind it is no more injurious in overdosage to the human economy than would be common salt when used in the same way."

Chittenden testified: "I know that my own experiments indicate that small amounts of borax produce no measurable effect that could be spoken of as deleterious; in fact, very small amounts tend to increase, if anything, the rate of digestion. That is especially true of boracic acid as contrasted with borax." This scientist states that one half of one per cent. of boric acid in butter is not objectionable.

Similar views concerning the harmlessness of borax and boric acid have been published in France by Laborde, Rondeau, and Vigier, and in Italy by Artimini and Polli.

Effect on Digestion.—Liebreich in Germany, Rideal and Foulerton in England, and Chittenden in this country have tested the effect of the presence of varying amounts of borax and boric acid on the salivary digestion of starch, and have reached practically the same conclusion, which is that borax slightly retards and boric acid slightly hastens the conversion of starch into sugar by ptyalin. On peptic digestion borax has no depressing effect until it is added to the extent of 0.2 per cent., and boric acid has an accelerating action until it reaches 1 per cent. According to Halliburton, boric acid has no influence on the action of rennin, but borax arrests the activity of this ferment when present to the extent of 0.1 per cent., or more. If, however, the acidity of the gastric juice is sufficient to convert borax into boracic acid the retarding action is not observed. Liebreich states that boric acid, even when present to the amount of three per cent., has no retarding effect upon the pancreatic digestion of starch, while borax does have some effect. Chittenden found that borax accelerates and boric acid slightly retards pancreatic digestion of proteins, and this conclusion has been confirmed by experiments made by Foulerton.

Thresh and Porter sum up the work that has been done on this subject as follows:

"Although too much stress must not be laid on experiments done *in vitro*, borax in small quantities appears to exert a markedly prejudicial effect on the action of rennin, and a slighter one on ptyalin; when present

in a greater proportion than 0.2 per cent. it also retards peptic digestion. Unless added in larger quantities it rather favors than retards the action of trypsin.

"Boric acid, on the other hand, has no action on rennin, slightly retards the action of ptyalin, when present in the proportion of 1 per cent., but begins to retard the action of trypsin when present to the extent of 2 per cent. Of the two substances, therefore, boric acid is less likely, judging from these experiments, to exert a prejudicial effect on digestion than borax."

Effect on Mucous Membrane.—Liebreich narcotized dogs and studied the effects of solutions of different strengths on the gastrointestinal mucous membrane. He found that solutions of boric acid up to 5 per cent. had no irritating action, but that borax began to injure the epithelium as soon as the strength reached 2 per cent. He attributes this to the alkali, and states that a 1 per cent. solution of sodium bicarbonate has a like action. Furthermore, he found that 0.5 per cent. solution of sodium chlorid caused a distinct inflammation. From these investigations he came to the conclusion that boric acid is less irritating to the gastrointestinal epithelium than either saltpeter or common salt.

Animal Experiments.—The results of animal experiments for the purpose of determining the effects of borax and boric acid have been quite as conflicting as the opinions of medical men founded upon professional observation. Harrington fed six cats upon borated meat for some weeks, keeping the same number of controls on nonborated food. The daily dose varied from 0.544 to 0.857 gram, and the total amount from 28 to 112 grams. Of the 12 animals only three gave evidence of acute illness during the period. All of these belonged to the borax group, and one died at the end of the sixth week. The others were apparently healthy at the expiration of 19 weeks. The 11 alive at this time were killed and their organs, together with those of the animals that died, were properly prepared and examined microscopically. All those which had been fed upon borated meat showed kidney lesions similar to those found in man in subacute and chronic nephritis.

Annett gave to some kittens milk containing 80 grains of boric acid to the gallon, to others milk with half this amount of the preservative, while a series had milk without any addition. All were allowed to drink the milk *ad libitum.* By the end of the fourth week all those having the larger amount died after having become markedly emaciated. Those having the milk containing 40 grains of boric acid per gallon also became thin, and later died. All the controls remained healthy and increased in weight. The same investigator found that kittens three months old were not affected by milk containing 80 grains of boric acid per gallon. From his work Annett concludes that boric acid is especially harmful to the young and should not be permitted in milk or other food given to infants.

Liebreich gave to one dog 2, and to another 3, grams of boric acid daily. Vomiting occurred on the 12th and 15th days, but the dogs continued in apparent health, and after 36 days one had gained 260 grams in weight, and the other had lost nothing. To a third dog he gave 5 grams of borax daily for 90 days. On the 16th day there was some gastrointestinal irritation, but the feeding was continued, and at the close of the three months the animal had gained more than 3 kilos. Three rabbits had each 0.3 gram of boric acid daily for one month, and gained from 30 to 100 grams. From these experiments Liebreich concluded: (1) There was no loss in weight, (2) there was no reduction in the absorption of fat, (3) there was a slight increase in the fecal nitrogen, possibly indicating that protein absorption was lessened, and (4) the borax, and not the boric acid, made the urine alkaline.

Hall, Hammond, and Tunnicliffe used suckling pigs that were 2 months old when the experiment was begun. Half of these received from 3 to 37 grains of boric acid each daily for 9 weeks, while the controls had the same food without the preservative. During the last 20 days the feces were collected and the nitrogen and fat determined. There were no appreciable differences between those fed on boric acid and the controls. At the end of this period both sets had gained equally, and there was no evidence of diminished absorption of proteins or fats. Chittenden and Geiss made an elaborate research on the effects of boracic preparations on metabolism. The animals were first seen to be in a state of nitrogenous equilibrium, an important point apparently neglected by some other investigators. Then all the food was measured and weighed, and all the excreta collected and analyzed. The conclusions reached by these investigators are stated as follows:

"Moderate doses of borax up to 5 grams per day, even when continued for some time, are without influence upon proteid metabolism. Neither do they exert any specific influence upon the general nutritional changes of the body. Under no circumstances, so far as we have been able to ascertain, does borax tend to increase body weight or to protect the proteid matter of the tissues.

"Large doses of borax, 5 to 10 grams daily, have a direct, stimulating effect upon proteid metabolism, as claimed by Gruber; such doses, especially if continued, lead to an increased excretion of nitrogen through the urine, also of sulphuric acid and phosphoric acid.

"Boric acid, on the other hand, in doses up to 3 grams per day, is practically without influence upon proteid metabolism and upon the general nutrition of the body.

"Borax, when taken in large doses, tends to retard somewhat the assimilation of proteid and fatty foods, increasing noticeably the weight of the feces and their content of nitrogen and fat. With very large doses there is a tendency toward diarrhea, and an increased excretion of mucus.

Boric acid, on the contrary, in doses up to 3 grams per day is wholly without influence in these directions.

"Borax causes a decrease in the volume of the urine, changes the reaction of the fluid to alkaline, and raises the specific gravity, owing to the rapid elimination of the borax through this channel. Under no circumstances have we observed any diuretic action with either borax or boric acid. The latter agent has little effect on the volume of the urine.

"Both borax and boric acid are quickly eliminated from the body through the urine, twenty-four to thirty-six hours being generally sufficient for their complete removal. Rarely are they found in the feces.

"Neither borax nor boric acid has any influence upon the putrefactive processes of the intestine as measured by the amount of combined sulphuric acid in the urine, or by Jaffe's indoxyl test. Exceedingly large doses of borax are inactive in this direction, not because the salt is without action on microorganisms, but because of its rapid absorption from the intestinal tract.

"Borax and boric acid, when given in quantities equal to 1.5 to 2 per cent. of the daily food, are likely to produce nausea and vomiting.

"Owing to the rapid elimination of both borax and boric acid no marked cumulative action can result from their daily ingestion in moderate quantities.

"At no time in these experiments was there any indication of abnormality in the urine; albumin and sugar were never present."

As has been pointed out by Chittenden and Geiss, the experiments of Cyon, Gruber, and Forster gave contradictory results. Cyon (14) concluded that borax, even to the extent of 12 grams per day, may be taken by dogs not only without the slightest disturbance, but with increased protein assimilation. On the other hand, Gruber (24) arrived at the diametrically opposite conclusion that borax causes increased disintegration of protein tissue, and Forster (19), not agreeing with either, decides that borax has no effect upon protein metabolism.

Tunnicliffe and Rosenheim (71) tested the effect of borax preparations on three children, two healthy boys, two and one half and five years of age, and a delicate girl, recently recovered from pneumonia, aged four. The food, which consisted of milk, bread, butter, meat, and fruit, was carefully measured and weighed, and the excreta were collected and analyzed. The children were kept in a condition of nitrogen equilibrium. They were given borax, boric acid, and a mixture of the two, and the conclusions are stated as follows:

"*Boric Acid.*—(1) Small doses up to 1 gram a day exert in healthy or delicate children no influence upon proteid metabolism. The assimilation of the proteid food was improved in one healthy child. (2) The phosphorus metabolism was unaffected in all cases. The assimilation of phosphorus was in all cases improved. (3) The assimilation of fat was

not affected. (4) The body weight was increased in all cases. (5) The quantity of dry feces was not affected. Their nitrogen percentage was slightly decreased. (6) No inhibitory effect upon intestinal putrefaction could be demonstrated.

"*Borax.*—(1) Continued doses of 1.5 grams have no influence in healthy or delicate children upon proteid metabolism. The proteid assimilation was unaffected in healthy children, slightly depressed in the delicate child. (2) The phosphorus metabolism was not affected in healthy or delicate children. The assimilation of phosphorus was improved in all cases, the improvement being least marked in the case of the delicate child. (3) The fat assimilation was improved in the case of one healthy child and unaffected in the case of the others. (4) The body weight was increased in all cases; the increase was most marked in the case of the delicate child. (5) The weight of dry feces and their nitrogen and phosphorus percentages remained unaltered. (6) Borax tended rather to increase intestinal putrefaction.

"*Boric Acid and Borax.*—(1) Both boric acid and borax were quickly eliminated, no cumulative action being therefore probable. (2) Neither boric acid nor borax in any way affected the general health and well-being of the children."

Wiley (74) with his "poison squad" has made a voluminous report on the effect of boric acid and borax upon metabolism and the general health. Young men (selected from numerous volunteers, presumably on account of their good health, although apparently some had albuminuria to start with) were fed upon weighed and measured foods, and their excretions were collected and analyzed. The preservative was given once a day, in capsule; thus, the daily dose was not distributed through the food or even through the meals, but taken at one meal. Space will not permit any adequate statement of this extensive work, and we will content ourselves with giving Wiley's general conclusions and Liebreich's criticism of the work.

Concerning the effect of boric acid and borax upon general health, Wiley makes the following statements: "The most interesting of the observations which were made during the progress of the experiments was in the study of the direct effect of boric acid and borax, when administered in food, upon health and digestion. When boric acid, or its equivalent in borax, is taken into the food in small quantities, not exceeding half a gram a day, no notable effects are immediately produced. The medical symptoms of the cases, in long-continued exhibitions of small doses, or in large doses extending over a shorter period, show in many instances a manifest tendency to diminish the appetite and to produce a feeling of fullness and uneasiness in the stomach, which, in some cases, results in nausea, and a very general tendency to produce a sense of fullness in the head, which is often manifested as a dull and persistent headache. In addition to the uneasiness produced in the region of the stomach there ap-

pear in some instances sharp and well located pains which, however, are not persistent. Although the depression in the weight of the body and some of the other symptoms produced persist in the after periods, there is a uniform tendency manifested after the withdrawal of the preservative toward the removal of the unpleasant sensations in the stomach and head above mentioned.

"The administration of boric acid to the amount of 4 to 5 grams per day, or borax equivalent thereto, continued for some time results in most cases in loss of appetite and inability to perform work of any kind. In many cases the person becomes ill and unfit for duty. Four grams per day may be ingested, then, as the limit of exhibition beyond which the normal may not go. The administration of 3 grams per day produced the same symptoms in many cases, although it appeared that a majority of the men under observation were able to take 3 grams a day for a somewhat protracted period and still perform their duties. They commonly felt injurious effects from the dose, however, and it is certain that the normal man could not long continue to receive 3 grams per day.

"In many cases the same results, though less marked, follow the administration of borax to the extent of 2 grams, and even of 1 gram per day, although the illness following the administration of borax and boric acid in these proportions may be explained in some cases by other causes, chiefly grippe.

"The administration of borax and boric acid to the extent of one half gram per day yielded results markedly different from those obtained with larger quantities of the preservative. This experiment, Series V, conducted as it was for a period of 50 days, was a rather severe test, and it appeared in some instances a somewhat unfavorable result attended it. On the whole the results show that one half gram per day is too much for the normal man to receive regularly. On the other hand, it is evident that the normal man can receive one half gram of boric acid, or borax expressed in terms of boric acid, for a limited period of time without much danger or impairment of health.

"It is, of course, not to be denied that both borax and boric acid are recognized as valuable remedies in medicine. There are certain diseases in which these remedies are regularly prescribed for both internal and external use. The value which they possess in these cases does not seem to have any relation to their use in the healthy organism except when properly prescribed as prophylactics. The fact that any remedy is useful in disease does not appear to logically warrant its use at any other time.

"It appears, therefore, that both boric acid and borax, when continually administered in small doses for a long period, or even when given in larger quantities for a short period, create disturbances of appetite, of digestion, and of health."

Liebreich (48), after a critical review of Wiley's work, states his final conclusions as follows:

"Thus, the conclusion drawn from an exhaustive examination of the figures and reports drawn up by Dr. Wiley is that no injurious effect was produced by the administration of the boron preservatives. The symptoms of ill health noticed during the attendance at the borax table must be attributed to inefficient hygienic conditions and to an injudicious mode of administering the preservative, as well as in a few cases to an unsuitable choice of persons for this experiment, in spite of medical examination.

(1) "With regard to weight, Dr. Wiley assumes that a loss of weight resulted. The average loss of 680 grams is so slight that it need not be ascribed to the use of boric acid and borax, but can be explained by chance occurrences at the preservative table. Moreover, a loss of weight does not by any means always mean an injurious influence.

(2) "The experiments on metabolism were undertaken with no equilibrium of nutrition.

(3) "The five periods are too short to prove regularity in feeding.

(4) "The percentages of nitrogen and phosphoric acid in the food were constantly changing, consequently:

(5) "It is impossible to decide whether the excretion increased during the preservative period.

(6) "Dr. Wiley calculates the elimination of phosphoric acid in percentages. This method of reckoning is a fault in calculation when the supply of phosphoric acid is not constant, the more so that Dr. Wiley's figures are obtained promiscuously from positive and negative phosphoric acid balances in the five periods.

(7) "On considering the separate tables we see that in the rise and fall of the elimination of phosphoric acid there is no connection between the magnitude of the dose of the preservative, or the number of days in the preservative period, and the amount of elimination of phosphoric acid.

(8) "The hygienic arrangements were not on a scale to do justice to every individual.

(9) "The medical supervision and self supervision were not sufficient for experiments of this kind.

(10) "The administration of the preservative, that is, of borax and boric acid, in capsules, allows of no conclusions as to the effects of borates when added to food.

(11) "It is not necessary to go into the question of calories. Wiley's own words explain this best. He says: 'The data are not wholly decisive, but very suggestive.' He does not say why they are suggestive, and he himself adds that his investigations were not thorough enough.

(12) "No lasting injury to health was found in spite of transient disturbances caused by the room used for experiment and the administration of the borax compounds in capsules. On the contrary, all the persons de-

clared themselves to be in better physical condition after seven months than they had been before."

The Preservative Properties of Borax and Boric Acid.—While toxicologists are quarreling about the effects of borax and boric acid upon the animal's body, we may find it both more pleasant and more profitable to turn to another aspect of the question and learn to what extent and under what conditions these bodies do preserve foods. It will be best to consider the preservative effects of the boron preparations on certain foods. They are added to milk to keep it sweet. The souring of milk is due to the growth and multiplication of the lactic acid bacillus, which converts the milk sugar into lactic acid. The rapidity with which milk sours depends principally upon two things: (1) The number of bacteria in it to start with. The cleaner a milk is, and the more care given to the cleanliness of the vessels in which it is kept and transported, the longer will the milk remain sweet. (2) The temperature at which it is kept. Within certain limits the higher the temperature at which milk is kept the quicker will it sour. Good clean milk when kept at 60° F. without any preservative will keep sweet about 48 hours, with 0.05 per cent. of boric acid it will remain sweet about 80 hours, and with 0.10 per cent. about 100 hours. At 65° F., without any preservative, good, clean milk will keep sweet about 36 hours, with 0.05 per cent. boric acid about 48 hours, and with 0.10 per cent. about 56 hours. At 80° the natural, clean milk will keep sweet 20 hours, with 0.05 per cent. of boric acid about 24 hours, and with 0.10 per cent. about 30 hours. It will be seen by these figures that the use of boron preservatives in milk is for the sole purposes of avoiding the expense and care necessary to keep the milk sweet, and the more cleanliness is neglected, and the less the attention given to refrigeration, the more of the preservative must be added to keep the milk from souring. Moreover, and what is more important, while boron preservatives retard the growth of the lactic acid bacillus, they have in the above given percentages no such effect upon the colon, typhoid, and other toxicogenic bacilli. Such preservatives, therefore, when used in milk, take down the danger signal without removing the danger, and their use in milk should be absolutely prohibited, and this should be done without any reference to the possible injurious effects of the borax preparation itself upon the consumer of the milk.

It also seems that there can be no question concerning the desirability of absolutely interdicting boron and all other chemical preservatives in canned food. The objects in such additions are twofold. (1) To preserve the food until it is sterilized by heat in the process of canning, and (2) to prevent the decomposition of the contents of the can in case the sterilization by heat is defective. The food manufacturer should not be permitted to add a preservative for either of these purposes, and to advertise fresh meat canned when in reality the contents of the can consist of bits

preserved by chemical agents, and subsequently canned, is to practice fraud which the law should prohibit and punish when done in violation of the law.

There are other instances in which the desirability of absolutely prohibiting the use of boron preservatives is not so clear. We will give only one illustration of this kind. Hams, sides of bacon, and cured fish, when transported through long distances, or kept for weeks in warm weather, are often sprinkled with boric acid, or, more properly speaking, packed in this substance. It has been shown experimentally that boric acid is especially valuable in preventing the development of aerobic bacteria, and when sprinkled on meat it penetrates slowly, and at the same time prevents the growth of bacteria on the surface of the meat. When meat thus preserved reaches the consumer much of the boric acid which exists as a dry powder on the surface is brushed off, and more of it is removed by the overnight soaking to which such meats are generally subjected. At present it seems that it would be wiser to regulate, rather than prohibit, this use of the boron preservatives. There should be a maximum limit, and all such food should be labeled "borated."

Potassium Chlorate

Symptoms.—Fortunately potassium chlorate is not so generally used as it was twenty years ago, because it has been found to be highly poisonous. It owes its poisonous action to the fact that it converts the hemoglobin of the blood into methemoglobin. The readiness with which this action takes place depends upon several conditions. The higher the temperature the more rapidly is the poisonous action manifested; therefore potassium chlorate is especially harmful when administered in fevers, exactly the condition in which formerly it was most generally prescribed. In the second place, decreased alkalinity of the blood favors its poisonous action, and the dyspnea which often accompanies throat affections, in which this salt has been so widely used, decreases the alkalinity of the blood by interfering with the elimination of carbonic acid gas. In the third place, the density of the blood influences the poisonous action, and by the addition of such indifferent substances as sodium chlorid and sugar the intensity of the effect is increased. When relatively small doses of the poison are administered the transformation of hemoglobin begins within the corpuscle, but with larger quantities the equilibrium between the formed elements and the plasma is destroyed, the corpuscles go to pieces, and the transformation continues in solution. The débris of the disintegrated corpuscles accumulates in various organs, interrupting their functions, and at the same time, the oxygen-carrying power of the blood being diminished, disturbances of metabolism result. In acute poisoning, which has resulted from mistaking the chlorate for purgative salts and swallow-

ing large quantities in a fasting condition, death results in a few hours. Vomiting, diarrhea, dyspnea, marked cyanosis, and weakness of the heart are the most prominent symptoms. In such cases the only constant change found after death is that resulting from the action of the poison on the red corpuscles. In less acute cases, such as have been observed from its excessive use in throat affections, the detritus resulting from the disintegration of the red blood corpuscles will be found collected in such organs as the kidney, spleen, liver, and bone marrow. Even the corpuscles which are not broken up appear as though they contained nuclei. The bone marrow is brown, and filled with disintegrated corpuscles. Both the straight and convoluted tubules of the kidneys are filled with cylinders made up of cellular detritus. Ide (31) reports the case of a man who, on account of a sore throat, swallowed twenty lozenges of potassium chlorate, six grains in all. After a few hours he suffered from abdominal pain, vomited and passed dark stools. The next day he was markedly cyanotic and passed only a small amount of urine which contained albumin and hemoglobin. Later coma developed, and death occurred eight days after taking the poison.

Bismuth Subnitrate

Symptoms.—It is still a question whether or not chemically pure bismuth subnitrate ever manifests poisonous action. This substance, which is largely employed in medicine, may contain traces of arsenic. However, the percentage of arsenic present is, according to Chittenden, very small, varying from 0.004 to 0.07 of one per cent. In cases of arsenical poisoning the plea is often made by the defense that the arsenic found by the chemist is due to the presence of this substance in bismuth subnitrate administered to the victim medicinally. It is needless to say that this claim should not have the slightest weight when arsenic is found in any weighable quantities.

Dalche (15) reports two cases of chronic poisoning from bismuth subnitrate applied to raw surfaces. In the first case a bismuth dressing was applied externally, for an extensive burn of the third degree, daily for one month. The first untoward symptoms which might be attributed to the bismuth appeared about the expiration of the second week, when a false membrane appeared on the uvula and tonsil. Underneath this membrane the tissue was black, and two days later a deep brown line was observed along the gums of the lower jaw. This remained permanent, and during the fourth week grave symptoms appeared. The stomach became exceedingly irritable, and vomiting was induced by both foods and medicines. A severe diarrhea set in, and the urine was found to contain a large amount of albumin. Although the dressing was discontinued at the end of the fourth week, for the reason that bismuth was found in the urine, and was

now suspected of being the cause of the untoward symptoms, the condition of the patient gradually grew more serious. The gums were shrunken and many of the teeth were loosened, while the alimentary canal seemed to be stripped of its mucous membrane in patches from the mouth to the anus. However, the patient finally recovered. In the second case an amputation above the knee was freely dressed with powdered bismuth subnitrate. Fifteen days after this dressing was begun salivation appeared, and shortly afterward there was a well-marked stomatitis. In this case also a blackish blue line was found along the gums. Bismuth was detected in the urine, and led to the suspicion that the dressings were causing the trouble. When these were discontinued recovery gradually followed. A thorough chemical study of the powder in both of these cases showed that the subnitrate was absolutely pure, with the exception of the fact that it contained traces of the oxychlorid of bismuth. It was suggested that in both of these instances bismuth was dissolved by the purulent secretions of the wounds, probably with the formation of an albuminate.

As early as 1882 Kocher (38) reported upon the injurious effects that may follow the dusting of wounds with bismuth subnitrate. In such a case he observed that the mucous membrane of the mouth became dark, the coloration beginning about the teeth; diarrhea set in, and a desquamative nephritis followed. It is worthy of note that it was Kocher (37) who recommended bismuth subnitrate as dressing for wounds, but it was soon found unsuitable for this purpose because it forms irritating concretions, and, as first pointed out by Kocher himself, it is not free from poisonous effects when thus employed. Petersen (57) reported a case of bismuth poisoning from the use of subnitrate, and, similar cases being observed, the employment of this agent as a surgical dressing has been largely abandoned. However, bismuth subnitrate is still occasionally used as a dusting powder, especially after extensive burns, and instances of poisoning following this use have been observed by Mühlig (51), Dressmann (17), and Don (16). The last mentioned authority also reports a case in which a severe stomatitis followed 36 hours after the injection of bismuth paste into an abscess cavity at the knee.

The more recent employment of large quantities of bismuth subnitrate by the radiographer has demonstrated that acute, fatal poisoning may result. Bennecke and Hofmann report a case in which three grams of bismuth subnitrate mixed with 100 c. c. of buttermilk was introduced into the stomach of a child three weeks old. Some twelve hours later the child became cyanosed, collapsed, and died. Similar cases have been reported by Böhme and others. It has been suggested that the untoward effects in these cases are due to the reduction of nitrate to nitrite by bacterial agencies. Indeed it has been demonstrated that when the colon bacillus is grown in beef-tea in which bismuth subnitrate is suspended reduction occurs and nitrite is formed. The cyanosis, sudden collapse, and methe-

moglobinemia found in these cases are conditions that are quite characteristic of nitrite poisoning. Beck (3) concludes a review of this subject as follows: "In the presence of certain bacteria in the feces of children bismuth subnitrate will liberate nitrites, which will be absorbed by the intestines and eliminated by the kidneys, and if the production is faster than the elimination methemoglobinemia will result. In large doses by mouth it is liable to produce an acute nitrite poisoning characterized by cyanosis, collapse, methemoglobinemia, and may terminate fatally. Rectal injection of small doses may cause nitrite poisoning much quicker and more severe than when administered by mouth. Children are more susceptible to nitrite poisoning due to administration of bismuth subnitrate. Persons suffering with intestinal putrefaction are very susceptible to nitrite poisoning when bismuth subnitrate is injected into the bowels. Bismuth injected into sinuses may be gradually absorbed, and ultimately find its way into the liver, spleen, muscles, and intestine. Black borders on the gums, ulcerations of mucous membranes, diarrhea, and desquamative nephritis may appear several weeks following the injection of the paste. After the introduction of large quantities of bismuth paste into suppurating sinuses mild symptoms of nitrite intoxication may appear. Acute nitrite poisoning is to be regarded as a distinctly separate affection from the more chronic bismuth absorption. Radiographers should employ some other preparation of bismuth than the nitrate, and refrain from injections of subnitrate into the bowels, especially if intestinal putrefaction is present."

The Mineral Acids and Inorganic Gases

The local effects of the mineral acids are dependent upon concentration rather than upon the amount. When applied to the skin or brought in contact with the mucous membrane the undiluted mineral acids destroy the tissues. When applied during life the area of contact is soon surrounded by one of inflammation, but when applied after death, while the tissue is destroyed, there is no evidence of inflammatory action. Usually when concentrated mineral acids are swallowed the mouth and stomach show the most marked effects, and the esophagus may escape with only slight irritation. However, in exceptional cases the lower part of the esophagus suffers most severely, and perforation just above the cardia has been observed. When the volume swallowed is not large the acid passes down the esophagus and along the smaller curvature of the stomach toward the pylorus, and in these cases the most noticeable changes will be found along this line, and the frequency of pyloric ulceration and stenosis after poisoning with the strong mineral acids is thus explained. When the changes induced in the stomach are not sufficient in and of themselves to cause death the gastric juice may digest the portions of the walls over which

the mucous membrane has been destroyed, and in this way late perforation may occur. It should be plainly stated, however, that the poisonous effects of the mineral acids are not wholly confined to local destruction of tissue; they may cause death by diminishing the alkalinity of the blood. In order that this result may follow it is by no means necessary that the blood in the peripheral vessels should lose its normal alkalinity, inasmuch as death would occur almost immediately after coagulation of the blood in the larger vessels. The life of herbivorous animals is easily jeopardized by increasing the amount of acid introduced into the body; while the carnivorous animals and man may bear relatively large quantities of acid, provided it be administered in sufficiently dilute form. This difference is explained by the fact that carnivorous animals may, in case of need, supply a large amount of ammonia which will neutralize the acid. Indeed, the greater part of the nitrogen which is eliminated by man in health in the form of urea may, under certain conditions, appear in the urine in the form of ammonia combined with some acid. The benefit to the animal body derived from its ability to furnish an alkali with which acids may be neutralized is seen in some forms of diabetes, in which the quantity of oxybutyric acid formed in the organism is large.

The administration of the mineral acids with murderous intent is seldom practiced, and the victims in the few cases that have occurred have generally been insane persons or young children. The larger number of deaths resulting from the administration of the strong mineral acids is found among suicides. It seems that the extensive destruction induced by these agents has a fascination for the diseased mind intent on suicide. The stronger mineral acids, especially sulphuric, have occasionally been used for the purpose of disfiguring the face. Accidental death from the strong mineral acids is an occasional, but somewhat rare, occurrence.

Sulphuric Acid

Symptoms.—When brought in contact with the skin concentrated sulphuric acid causes marked pain, and the area of application becomes at first white and then brown. After a few minutes the adjacent skin becomes red and swollen. The epidermis is destroyed instantaneously, and the destructive action may extend to the deeper tissues. Suicides in attempting to swallow concentrated sulphuric acid often find themselves unable to do so on account of spasm of the pharynx, and the fluid poured into the mouth runs out over the chin and neck. When the area of skin destroyed by concentrated acid is great intestinal ulceration develops as it does after extensive burns, and the individual falls into a somnolent condition terminating in coma and death. This is undoubtedly due, as it is in the case of extensive burns, to alterations induced in the blood. When concentrated sulphuric acid is thrown into the eyes conjunctivitis and

keratitis result, and these are frequently followed by glaucoma, which leads to blindness.

When death is accomplished by swallowing the acid brownish marks are frequently seen extending from the corners of the mouth over the lower jaw and down upon the neck. Frequently the lips are excoriated and may be burned brown or even black. The mucous membrane of the mouth and tongue is covered with a white, grayish, or brownish layer of altered tissue. The concentrated acid actually burns and destroys the histological elements of the mucous membrane. In the stomach similar changes are found, but the destructive action is frequently deeper than it is in the mouth. The walls may be pierced, and the effects of the acid may be seen on adjacent organs. Perforation has been reported in about one-third of the cases, but is dependent upon the strength and amount of acid reaching the stomach. Black and charred spots, consisting of decomposed blood pigment, may be seen in the stomach, and in case of perforation in the peritoneal cavity. Alterations in the intestines resemble those in the stomach, but are less intense, and gradually grow less marked in the lower portions. If life be not immediately destroyed parenchymatous inflammation may develop in the liver and kidneys.

Fagerund reports seven deaths from sulphuric acid. Two were murders, four were suicides, and one was accidental. In one of these a servant administered to an insane woman a wineglassful of concentrated sulphuric acid. Severe vomiting immediately followed, and death occurred within sixty hours. Section showed brownish spots on the chin and hands. The tip of the tongue was ulcerated, and marked ecchymoses were found throughout the mouth, esophagus, and along the larger curvature of the stomach. In the second case of murder a mother administered an unknown quantity of concentrated sulphuric acid to her illegitimate child. Death occurred within a few hours, and post-mortem examination showed extensive destruction of tissue in the pharynx, esophagus, and stomach. In two of the cases of suicide death occurred in about twelve hours, and the mucous membrane of the tongue, pharynx, esophagus, and the upper part of the small intestine was found to be extensively destroyed. In one of the suicidal cases the acid was taken with the belief that it would induce abortion. Death did not occur until about fourteen days after the acid had been taken, and was due to the local destructive action of the poison. In the accidental case a man drank sulphuric acid, supposing it to be brandy. The mucous membrane of the tongue was destroyed, while that of the esophagus was dark gray in color, and the stomach contained half a liter of dark fluid blood.

Chronic poisoning with dilute sulphuric acid is rare, and probably does not occur in this country. Kobert states that sulphuric acid is sometimes added to brandy, and also to wine, in France in order to improve the taste of these drinks and to make them "bite." In animals experi-

mentally poisoned with dilute sulphuric acid there is an increased elimination of lime salts in the urine. Dilute sulphuric acid is sometimes added to wine for the purpose of precipitating the gypsum, and it is possible that the acid sulphate of lime thus formed, together with traces of free acid, may be a source of danger to life. According to Kobert, acid sulphate of lime is an important factor in death from inanition in herbivorous animals, inasmuch as the sulphuric acid which results from the oxidation of the sulphur of the protein tissue is insufficiently neutralized. According to the same authority, so-called neutral sulphate of potassium may cause death. In such cases section shows the stomach and intestines inflamed, and these effects are attributed to the presence of the acid sulphate or to other impurities.

Treatment.—In case of poisoning with sulphuric acid any of the alkaline carbonates properly diluted may be administered; or chalk or calcined magnesia may be given suspended in milk or water. It should be understood, however, that after the acid has destroyed tissue neutralization will not repair the damage done. It can only prevent the further action of the poison.

Sulphurous Acid and the Sulphites

Properties and Uses.—Sulphurous acid is known and used as the anhydride, or in the form of a sulphite. The gas has many useful applications, some of the most important of which are the following: (1) It is largely employed as a disinfectant for rooms and their contents after infectious diseases. This use, however, is being superseded in part by formaldehyde, which is more easily managed, and for most purposes quite as efficient. (2) It is used as a bleaching agent, especially for textures made of straw and bark. (3) Sulphur is burned in empty wine casks, preparatory to refilling, in order to destroy bacteria and molds. Inasmuch as this introduces a small amount of sulphite into the wine, many attempts have been made to discover some suitable substitute for burning sulphur, but, so far, without success. The German law, which is quite stringent against the addition of sulphite to food, permits the disinfection of wine casks with burning sulphur. (4) Dried fruits, apples, and pumpkins are sometimes treated while in course of preparation with the vapor of burning sulphur. The moisture in the fruit absorbs the sulphur oxid, which acts as a preservative. (5) The acid sulphites are employed extensively in the preparation of wood pulp for the manufacture of paper, "the sulphite process" being used at the present time to the practical exclusion of all others. (6) The sulphites have been widely used as food preservatives. Sodium sulphite, often mixed with boric acid or borax and sodium bicarbonate and sold under some fanciful name, such as "XXX preservative," is the salt most generally employed, and it finds its widest application to

the so-called Hamburger steaks. These are made by taking the bits that accumulate about the meat block, passing them through a sausage grinder and sprinkling with the preservative. In Pennsylvania there have been many arrests for this form of food adulteration, and conviction has generally resulted because there has been no difficulty in showing that the salt, even in relatively small doses, is a potent poison.

Poisonous Effects of the Gas.—In 1883 Ogata (53) made a study of the effects of sulphur dioxid on rabbits, guinea-pigs, and mice. He found that these animals could be exposed to an atmosphere containing 0.4 per cent. volume without permanent injury, but that it caused dyspnea and corneal cloudiness which persisted for some days. Two years later Lehmann (45) continued these investigations and studied the effects of the gas on men, those unaccustomed to it and those who worked in a wood pulp factory. He found that the former could breathe without marked discomfort an atmosphere containing 0.02 per cent. volume of the gas, but when the amount was increased to 0.03 or to 0.04 per cent. continued stay in the room was impossible. However, the workmen in the pulp factory breathed this atmosphere without being conscious of any harm, and they were found to be quite healthy. The air in the factory varied in SO_2 content in different parts, and at different times of the day from 0.0065 per cent. to 0.0367 per cent.

Effects of Sodium Sulphite on Animals.—If 10 c. c. or more of a 10 per cent. solution of sodium sulphite be introduced into a rabbit's stomach through a tube the animal soon springs from the floor once or twice, then falls, and in a few minutes is dead. Section shows the following conditions: The lungs are congested but otherwise normal. There may be small hemorrhages in the muscles of the heart. The mucosa of the stomach is highly inflamed and shows here and there hemorrhagic spots; it is easily detached from the deeper tissue. The mucous membrane of the small intestine is highly congested. The liver is markedly hyperemic and the kidney is also quite congested. But one may say with truth that a strong solution of common salt has practically the same effect, and that this does not show that the small amount of sodium sulphite added to meat as a preservative is harmful. We will therefore attempt to ascertain what the small quantities of this preservative may do.

Kionka (34) was the first to study the effects of the long-continued administration of meat treated with sulphite preservative on animals, and largely upon his report the German government was induced to enact a law forbidding the addition of sulphite to meat. This led to counter experiments, and in 1902 Kionka and Ebstein (35) repeated the investigations of the former, apparently with great care. They chose dogs for their subjects, and knowing that Pflüger had shown that dogs were seriously affected by an exclusive meat diet, especially one of horse flesh, they gave their animals good beef, mixed with bread and potatoes. Three dogs

received meat mixed with 0.2 per cent. sodium sulphite, and three had meat treated with 0.1 per cent. of a sulphite preservative. The animals were well cared for, being kept in roomy, well-lighted and ventilated cages, and given exercise out of doors in good weather, and in the room at other times. The meat was freshly prepared each day. This feeding was continued for from 64 to 67 days, and then, after two days on food without preservative, the animals were killed by opening the carotid. In two dogs the blood was washed out with a 0.75 per cent. sodium chlorid solution. During the whole period the animals were apparently in good health. The appetite and stools were normal, and at first all gained in weight, after which the weight remained constant. Only two of the dogs manifested anything worthy of note during the feeding, and these were pregnant bitches. As early as 1869 Bernatzik and Braun had reported upon the abortive action of the sulphite administered to pregnant women. On the 30th day of the feeding one bitch dropped a dead puppy, and later the other prematurely gave birth to four young ones, one of which was dead; two died soon after birth, and the other one on the 14th day. In both instances birth was followed by hemorrhage that lasted several days.

The dogs were carefully sectioned, and their organs, after proper preparation, were submitted to microscopical examination. Three showed hemorrhages in the lungs; four subendocardial hemorrhages; four hemorrhages of the pyloric portion of the stomach; three inflammation and hemorrhage in the intestinal mucous membrane, and all hemorrhagic nephritis. Other animals used in the same laboratory for other purposes and killed by the same method did not show these abnormalities. Therefore, the authors conclude that the sulphite was responsible for the lesions, and that it is a blood poison.

The above mentioned experiments and the conclusions derived therefrom have been criticized by Lebbin and Liebreich. The latter claims that dogs used in laboratories for experimental purposes are often unhealthy, and besides that an excess of meat in the food will cause the nephritis reported by Kionka and Ebstein. In his Philadelphia testimony this German savant stated: "The laws in Germany are not health laws, but they are political laws; everybody knows it, and the government itself will say that it is a political law." It must be admitted that some of the pure food laws in this country are also political rather than health laws.

Harrington (27), recognizing that about 25 per cent. of dogs kept in cages have nephritis, selected cats for his work. "Six cats were fed for twenty weeks, five receiving six feedings weekly of meat containing 0.2 per cent. of sodium sulphite, and the sixth receiving the same meat with no addition. The latter showed a constant gain in weight to the end; the others gained until about the ninth week, and then began to lose ground, frequently refusing food, or leaving it uneaten, but otherwise they showed no evidences of injury. At the end of twenty weeks they were killed with

chloroform, and examined by Dr. E. E. Tyzer, of the Department of Pathology of the Harvard Medical School. There was no macroscopic evidence that this chemical had produced any changes in the organs, but thin slices were cut from each of the organs of each cat, fixed in Zenker's fluid, and then imbedded in paraffin and cut. Eosin and methylene blue were used for general staining, and Mallory's stain was employed also. The microscopical findings were by no means so extensive as those yielded by Kionka's dogs. Indeed, apart from some slight, inconstant variations in the spleens, all of the organs of each animal were perfectly normal, with the exception of the kidneys, which, in all but the control, showed marked changes."

Schulz (64) fed three dogs on meat treated with 0.2 per cent. of a preservative preparation that contained 80 per cent. of sodium sulphite. The food was mixed, containing meat, fat, potatoes, and rice. At first horse flesh was given, but on becoming aware of the statement of Pflüger that horse flesh may be harmful to dogs beef was substituted. The experiment was begun Nov. 12, 1901, and continued until Jan. 27, 1902. Two of the dogs had diarrhea, accompanied by loss of appetite, and aversion to the food containing the sulphite. No. 1, which had retained apparent health, showed numerous hemorrhages in the lungs. Nos. 2 and 3 had marked gastrointestinal catarrh, and the inflammatory process extended into the submucosa, and indeed had involved the whole thickness of the intestinal wall. They also showed an inflammatory condition of the kidneys. Schulz concludes that these pathological conditions could have been due only to the sulphite.

The Preservative Action of Sodium Sulphite.—The addition of sodium sulphite to chopped meat is not, properly speaking, for the purpose of preserving the food. A food preservative is a substance added to a fresh, undecomposed food, in order to prolong the period that it may be kept good. As a rule the sulphite is not added to fresh meat, but to that which is already decomposed, and generally to such an extent that it would not be eaten by any one unless something were done to mask its real condition. In fact, the sulphite preservative is preferred to other meat preservatives, because, better than any other, it enables the dealer to dispose of products that he could not sell for food in any other way. The bits that have accumulated about the chopping block and which are already badly decomposed are ground, and then sprinkled with the preservative. The grinding brings out the color by exposing new surfaces and mixing the gray, sodden exterior of the pieces with the better looking interior, and the sulphite is added to hold the bright, normal color brought out in the grinding, and to hide the odor of decomposition. All admit that the sulphite holds the red color of the meat, but the one who favors its use will deny that it will restore the normal color once lost by decomposition, and in this he is probably right. It is the grinding that freshens

the meat in appearance, and the sulphite holds the color restored by the grinding. Decomposition continues, not so fast, it is true, after the preservative has been added. The more advanced the decomposition at the time of grinding the more of the preservative is added, because more is necessary to hold the color and to mask the odor. This is the reason why Stroscher (70) found the greatest number of bacteria in those samples of chopped meat that contained the largest per cent. of sulphite preservative.

Effects of the Sulphite on the Stomach and on Digestion.—That sodium sulphite taken into the stomach neutralizes the free hydrochloric acid cannot be denied by any one, and the only answer of those who hold that the use of this salt in food is harmless is that the amount of the preservative added is so small that any ill effect from the neutralization of the free acid is so slight that it may be disregarded. Fortunately, the neutralizing effect of the preservative may be easily calculated. A hungry man may eat at one meal 500 grams of meat, and this, if treated with the preservative at all, will contain not less than 0.2 per cent. of the sulphite. It may contain twice as much or more. One per cent. of 500 grams is 5 grams, and 0.2 per cent. is one gram. The normal gastric juice contains 0.2 per cent. of free hydrochloric acid. One gram of sodium sulphite will neutralize in round numbers 0.3 grams of hydrochloric acid, which is the amount in 150 c. c. of normal gastric juice. The amount of gastric juice poured out at each meal varies greatly, but suppose that it lies between 500 and 1,000 c. c., then from a little less than one-third to a little more than one-seventh of it will be neutralized by the preservative, and if one's capability of digesting food is thus reduced day by day and meal by meal for an indefinite period the injury done is by no means so small that it may be disregarded. However, the fact that the free acid of the gastric juice is neutralized and rendered inert is not the worst feature of the reaction between the salt and the acid. At the same time the sulphurous acid is set free and dissolved in the fluids of the stomach. Pfeiffer (58) has shown that very dilute aqueous solutions of this gas irritate and inflame the stomach, and when it reaches the proportion of 0.5 per cent. it causes a severe gastritis.

Nitric Acid

Symptoms.—This acid is largely used in various manufactures, and medical literature contains the records of about four hundred cases of poisoning with it, mostly accidental. Nitric acid colors the skin yellow, and this becomes orange on the addition of ammonia. The coloration of protein matter by nitric acid is known as the xanthoproteic reaction. When the acid is taken in solution of less than 20 per cent. the local effects are not prominent; but when the concentration reaches 33 per cent. or more the destructive action is similar to that of sulphuric acid. In the

intestines the mucous membrane is stained gray or grayish white, and this is regarded by Lesser as important in distinguishing between this acid and chromates. The stomach may be perforated and the abdomen distended by gas. When death does not occur immediately the kidneys show an acute parenchymatous inflammation. According to Bellin, nitric acid in daily doses of from 10 drops to 15 grams is used in Russia as an abortefacient. Chronic poisoning results from the treatment, and is characterized by tremor, insomnia, marked anemia, gastric catarrh, and diminished secretion of urine. In two cases section has shown fatty changes of the heart, nutmeg liver, enlargement of the spleen, nephritis, and effusion beneath the meninges of the brain. It is possible that some of these effects may have been due to arsenic in the acid.

Ipsen (32) reports a case of poisoning with nitric acid in which the lips and the visible portion of the mucous membrane of the mouth were stained yellow when the patient was first seen, an hour after she had swallowed a small bottle of fuming nitric acid. The face was cyanotic and the extremities cold. Respiration was greatly accelerated, the pulse was rapid, and pressure over the region of the stomach caused severe pain. It was found to be impossible to administer antidotes or to wash out the stomach on account of stenosis of the pharynx, which had already supervened. Cyanosis and dyspnea increased. Collapse became marked, and death resulted in three hours after swallowing the acid. Section showed that there had been perforation of the esophagus just above the diaphragm. The mucous membrane of the tongue, pharynx, and larynx was yellowish green, swollen, and easily detached from the subjacent tissue. The stomach was contracted, and the walls exceedingly brittle, but without perforation. Extensive injury had also been done to the upper part of the duodenum. Although, as stated above, there was no perforation of the stomach, acid was found in the peritoneal cavity, and the question arose as to whether or not strong nitric acid would penetrate the unbroken walls of the stomach. In order to decide this question Ipsen introduced a small quantity of nitric acid, diluted with an equal volume of water, into the stomach of a dead child. The body was placed in a cool cellar and left in a horizontal position for twenty-four hours. At the expiration of this time autopsy was made, and it was found that the acid had penetrated the walls of the stomach without perforation, and had stained adjacent portions.

Kockel (39) reviews fully the poisonous action of the vapors of nitric acid, which consist of oxids of nitrogen, and he also gives an index of the most important contributions to the literature of this subject. He reports a case of a man who broke a large carboy of nitric acid and remained in the room for one hour. The individual was sixty-five years old, and although he immediately complained of some dryness of the throat and showed some tendency to cough, these slight symptoms passed away, and

he felt quite well until six hours later, when he became short of breath, showed marked cyanosis, and died within a few hours. Experiments made with animals show like effects of this poison. A rabbit exposed for thirty minutes to the vapor of fuming nitric acid showed rapid breathing for fifteen minutes after removal from the gas, and then apparently wholly recovered; but thirty-six hours later died suddenly. Kockel holds that the symptoms from the inhalation of the fumes of nitric acid are typical and characteristic both in animals and in men, and that when the irritation is removed there is temporary recovery, followed by a reappearance of the rapid breathing and death.

Treatment.—The treatment of nitric acid poisoning consists in the administration of the carbonates of the alkalies or alkaline earths, and the subsequent administration of mucilaginous drinks. The statement which has already been made under the head of sulphuric acid, concerning the inability of antidotes to repair damage already done by the acid, holds good for this poison also.

Nitrous Acids and Nitrites

Laughing gas is not irritating, but is a nerve poison. The other gaseous oxids of nitrogen are highly irritating, and when inhaled they induce coughing, cyanosis, dyspnea, and dizziness, and when inhaled in small amount for a long time a purulent bronchitis may result. Frequently after inhalation of one of these gases the individual may feel quite well on withdrawal to a pure atmosphere, when some hours later there comes on a sense of suffocation which grows more and more distressing and is followed by convulsions, terminating in death, the intellect remaining clear to the last. Death is due to pulmonary edema. When the nitrites are swallowed the first effect manifests itself in irritation of the mucous membrane of the stomach and intestines, followed by blood changes, the formation of methemoglobin, and then come the evidences of action on the central nervous system.

Hydrochloric Acid

Symptoms.—As a result of swallowing hydrochloric acid stricture of the esophagus is frequent, while perforation of the stomach is rare. Lessèr (46) reports the following case: A man took a "small swallow" of hydrochloric acid of a strength of 24.7 per cent. two hours after he had eaten heartily. Vomiting immediately followed. There was total corrosion of the epithelium of the mouth, pharynx, and esophagus. A hemorrhagic gastritis was found, but the intestine had not been reached by the acid in sufficient strength to cause destructive changes. However, the reaction of the contents of the alimentary canal throughout was acid, and

emulsions of the liver, lungs, heart, and spleen were also acid. The same authority reports a case of death caused by taking 2.5 c. c. of hydrochloric acid mixed with 100 c. c. of syrup. After death about 300 c. c. of a strongly acid fluid was found in the stomach, and from this 130.5 mg. of hydrochloric acid was obtained.

Lehmann (43) found that an atmosphere containing one part or more per thousand of the vapor of hydrochloric acid causes in animals a flow of tears, conjunctivitis, and cloudy swelling in the cornea. The duration of exposure necessary to induce these effects varies with the ability of the animal to protect the eye by closure of the lids. The tears were found to be milky, and microscopic examination revealed the presence of fat globules, believed to come from the meibomian glands. The mucous membrane of the nose is inflamed, and some days after exposure a purulent nasal catarrh may set in and lead to dry necrosis, or a moist gangrene involving the septum and the alæ, and causing extensive destruction. This effect is supposed to be due to the local action of the gas on the blood supply to the parts. The salivary glands are greatly stimulated in some animals. When death occurred during the experiment or the animals were killed soon after exposure, the trachea was found to be pale and to show only a few ecchymoses. The bronchial tubes contained a thin frothy secretion. There was uniformly an emphysematous condition, and pneumonic changes were observed in animals that survived the exposure twenty-four hours or longer. In all the guinea pigs exposed to an atmosphere containing one part per thousand of the gas hemorrhagic spots were found in the mucosa of the stomach.

Chlorin and Bromin

According to Böhm, there had been, up to 1880, eleven cases of acute fatal poisoning with chlorin gas. Eulenberg states that the alveoli of the lungs are sometimes torn in coughing when chlorin gas has been inhaled, and fatal hemorrhage may result in this way. The severe coughing may also lead to rupture of some cerebral blood vessel and death from apoplexy. In other instances asphyxia comes on, and the individual falls into unconsciousness, and death follows. The researches of Lehmann (44) have shown that chlorin and bromin are qualitatively and quantitatively alike in their effects upon the animal organism, while they differ widely from the vapor of hydrochloric acid. The effects upon the eyes and the mucous membrane of the nose and mouth are much less marked than with the acid, and necrosis of the septum and alæ of the nose did not occur in any of Lehmann's experiments. The effects of these gases are most evident in the lungs, even when the atmosphere contained only 0.01 to 1,000 of either of these gases, and after an exposure of six and one half hours there developed, after twenty-four hours, a mucopurulent bronchitis with

pneumonic foci and marginal emphysema. Edema of the lungs was much more constant and pronounced than in either poisoning with ammonia or hydrochloric acid vapor. When the percentage of the gas was increased a typical croupous membrane developed, and in some instances was continuous from the larynx to the finest bronchi. When the amount of gas reached 0.3 to 1,000 and the exposure was continued for one hour or longer this membrane invariably appeared. Marked dyspnea and profound stupor were frequent symptoms.

Hydrogen Sulphid

Symptoms.—The frequency with which man is exposed to the action of this gas, which is one of the products of certain putrefactive bacteria, renders a study of its poisonous effects of great interest. Hydrogen sulphid, when given off from decomposing matter, is generally mixed with other gaseous products of putrefaction, such as carbonic acid gas, CO, and NH_3, and the effects may be exceedingly variable, according to the relative amount of each of these present. Furthermore, an atmosphere largely contaminated with these gases is relatively poor in oxygen, and this deficiency has its own ill effects. Accidental poisoning with pure hydrogen sulphid gas occasionally occurs in laboratories.

The injurious effects of hydrogen sulphid are undoubtedly not sufficiently appreciated by those who have neither tested its action nor acquainted themselves with the literature of the subject. The writer has repeatedly observed its effects in sterilized bacterial cultures, when its presence was hardly perceptible to the sense of smell, and when silver or lead paper placed over the test tube blackened very slowly; and yet such cultures have frequently been found to contain enough hydrogen sulphid to kill animals when injected in quantities of a few cubic centimeters into the abdominal cavity. It has been found that a very filthy water may yield simply on agitation 140 times its volume of hydrogen sulphid gas, and on being heated it may part with 46 additional volumes. It has been estimated that the amount of hydrogen sulphid that may be obtained from 1 cm. of water holding the above mentioned amount would be sufficient to render 28 cm. of air fatally poisonous to man. Dupuytrin and Thenard found that an air which contained 0.66 to 1,000 of this gas is poisonous to birds; one with 1.25 to 1,000, poisonous to dogs, and one with 4 to 1,000 is poisonous to horses. Biefel and Polek found that a rabbit died after 75 minutes' exposure to an atmosphere containing 0.59 to 1,000 of hydrogen sulphid gas, and that another rabbit died after an exposure of two hours to an atmosphere containing only 0.37 to 1,000.

Lehmann has made most valuable experiments upon the poisonous effects of this gas. He employed a Pettenkoffer-Voit respiration apparatus. All the animals used showed signs of local irritation after pro-

longed exposure to air containing only 0.13 to 1,000. A narcotic effect was shown by the position taken by the animals. Paralysis gradually developed and death resulted from failure of respiration. In cats death was preceded by a restless sopor. When the amount of gas in the air was increased to 0.72 to 1,000 the animals suffered greatly from dyspnea, while some were thrown into convulsions in which opisthotonos was marked. In all of these cases death was not due to paralysis of the nerve center solely, but in part to simultaneous changes in the lungs. At first respiration became slow; then, with increasing dyspnea, it grew in rapidity. Section showed edema of the lungs in all animals which had been exposed to the action of the gas for some hours. The lungs were voluminous, diffusely dark red, and showed punctiform blood extravasations. The fluid of the edematous lungs was very abundant, stained with blood, and even ran from the mouth after death. Marginal emphysema was seldom absent, and in some instances was highly marked. Pleuritic effusions were frequently observed. When animals or men are exposed to an atmosphere containing a large amount of hydrogen sulphid death may be instantaneous. In these cases no constant lesions are found. The blood is generally fluid and dark in color.

Treatment.—The treatment for poisoning with hydrogen sulphid consists in removal to good air, and the persistent employment of artificial respiration. Hydrogen sulphid, when present in harmful quantities, is usually recognizable by its distinctive odor. Chemically it may be detected by its blackening silver coin or lead paper.

Carbon Monoxid

Symptoms.—Carbon monoxid is the most poisonous constituent of illuminating gas. It has caused many deaths, and probably is responsible for many which have been attributed to other causes. It is largely employed for suicidal purposes, and cases of accidental poisoning with it are by no means rare. Illuminating gas made from coal contains from 5 to 10 per cent. of carbon monoxid, while that made from wood may contain as much as 60 per cent. Water gas, now so largely used for illuminating purposes, contains about 30 per cent. There has been some difference of statement concerning the amount of this gas necessary to render harmful the inhalation of air containing it. The most exact experiments place the amount at about 0.02 per cent. The deadly effects of carbon monoxid are due to the readiness with which this gas combines with hemoglobin, and to the stability of the compound thus formed. The affinity of carbon monoxid for hemoglobin is about two hundred times greater than that of oxygen. It will be seen from this that when the inhaled air contains only traces of carbon monoxid it is retained and may accumulate in the blood. It should be plainly understood, however, that even in fatal poisoning with

this gas the greater part of the hemoglobin in the body remains in combination with oxygen. The writer saw some few years ago a report of a case of poisoning with carbon monoxid in which the statement was made that there was no oxyhemoglobin left in the blood, and yet this was not a fatal case, and, according to the author of the paper, the patient continued to live up to the time of the report, some months after exposure to the gas, without any oxyhemoglobin in his body. It is needless to say that such a statement as this is absurd. Death results when the respiratory capacity of the blood is reduced from 20 to 30 per cent., and saturation of the hemoglobin of the blood with carbon monoxid during life is impossible.

With proper treatment persons poisoned with this gas, even to the extent of complete insensibility, may recover. In such cases recovery is due to the slow dissociation of the hemoglobin compound. The corpuscles, the hemoglobin of which is combined with carbon monoxid, retain their normal form, and are not immediately disintegrated, but are destroyed more quickly in the liver than are those corpuscles the hemoglobin of which is in the normal condition. From his experiments Dresser concludes that a fatal quantity of carbon monoxid for a man weighing seventy kilos is about 0.8 gram. The whole of the gas inhaled is not held by the hemoglobin. Some of it is dissolved in the blood plasma, and some of it penetrates the tissues and, according to Fehling, may pass from the mother to the fetus.

Inasmuch as carbon monoxid hemoglobin gives off no oxygen to the tissues, the symptoms are practically those of asphyxiation. Blood containing this gas is of a cherry red color, and this peculiar characteristic tint may in many instances be observed several days after death. The spectrum of carbon monoxid hemoglobin exhibits two dark bands between the lines D and E, and is similar to the spectra of oxyhemoglobin and hemoglobin. However, these are not identical, and with all of them in view can be easily distinguished one from the others. The oxyhemoglobin spectrum lies farthest to the left; that of hemoglobin farthest to the right, extending slightly beyond E; while that of carbon monoxid lies between. Furthermore, the lines of the carbon monoxid compound are not so widely separated as those of the oxyhemoglobin spectrum. Moreover, the addition of a reducing agent to normal blood speedily alters its spectrum, while this does not happen when one-fourth or more of the coloring matter is combined with carbon monoxid.

Besides its indirect effect on the tissues by interrupting the oxygen-carrying power of the blood, carbon monoxid is a direct poison and capable of inducing marked destructive changes. Primarily the heart beats slowly and violently, and rupture of the blood vessels may occur during this stage. Secondarily, the heart beats rapidly and feebly. The latter is the period of vasomotor paralysis, and as a result of this condition bright red areas appear on the surface. When not seen until after death these

are usually mistaken for post-mortem effusions. However, they may occur in those who ultimately recover. Among the first symptoms are occasionally observed abnormal motility and violent convulsions. Later there may be extensive paralysis. In about 70 per cent. of the cases of poisoning with this gas the urine contains a reducing substance, which, in some instances, has been found to be sugar, while, in others, it has been reported as glycuronic acid. A test for reducing bodies in the urine may serve as an aid to diagnosis in doubtful cases, and it might be remarked that albumin is present in about 20 per cent., and that lactic acid appears in the urine in cases of severe poisoning.

In acute poisoning with carbon monoxid the color of the blood is supposed to be pathognomonic. The skin is stained over limited areas, and the soft tissues, such as the muscles and viscera, are rose red. Kobert makes the statement that the carbon monoxid hemoglobin has been detected in the body 18 months after death. The blood corpuscles retain their form some time after death, and the arteries are generally full. Ecchymoses in the meninges and capillary hemorrhages in the brain have been found. Pneumonic changes in the lungs are frequently observed, and fatty alterations in the kidney, liver, and heart have been reported. Ziemsen found a diphtheritic-like exudate on the gums, in the trachea, colon, and rectum. Gangrene of the muscles of the neck has been reported, and deep bedsores have been known to form in a very short time.

In chronic poisoning with carbon monoxid numerous and extensive extravasations may occur. Marked anemia is frequently observed, and is due in part to the rapid destruction of carbon-monoxid-bearing corpuscles in the liver, and in part to the nephritis that comes from the elimination of the decomposing products. In dogs chronically poisoned with this gas the epithelium of the convoluted tubules undergoes necrotic changes, and may be stripped off altogether. The enormous increase in nitrogenous metabolism with muscular degeneration is surpassed only by phosphorus poisoning.

Hydrocyanic Acid

Properties.—Pure hydrocyanic acid is a colorless, volatile liquid, known only in the laboratory. It is usually made by distilling one of the salts with some dilute mineral acid, such as hydrochloric or sulphuric. The pharmacopeial preparation is a two per cent. solution, but on account of the instability and volatility of the acid the preparation that generally stands under this label in the drug store is inert, and probably this is fortunate since the poisonous action is so prompt and the therapeutic effect so doubtful that it should not be prescribed at all. The aqueous solution when exposed to the light soon decomposes with the formation of a brownish residue of unknown composition. The tendency to decomposition is

retarded by the presence of traces of mineral acid, and dilute sulphuric acid is sometimes added for this purpose. There is a preparation known as Scheele's acid that is supposed to contain as much as five per cent., but often falls short of that amount. This solution may be preserved, or at least its decomposition may be retarded, by using a 20 per cent. glycerin solution instead of water as a solvent. Wormley (75) examined several specimens of commercial hydrocyanic acid and found none more than 1.5 per cent., and in one which had not been opened since leaving the manufacturer he found none.

Of the inorganic compounds of hydrocyanic acid the cyanids of potassium, mercury, silver, and gold are the ones best known and most generally employed. The first mentioned has been largely employed as an insecticide, and the others in plating metal. All are poisons, and most accidents due to this poison result from the use of this salt rather than from the free acid. The hydrocyanic group is a constituent of many organic bodies found in both the vegetable and the animal world. It is contained in numerous glucosids, some of which carry a ferment by which, under favorable conditions, the poisonous body is set free. The best known example of this is the amygdalin of the bitter almond, the decomposition of which leads to the production of free hydrocyanic acid. The ferment that induces this reaction is known as emulsin, and the amygdalin is broken up into glucose, hydrocyanic acid, and the oil of bitter almond. The oil, or benzaldehyd, is, when freed from the hydrocyanic acid, used as perfume. Instances of poisoning with benzaldehyd have been reported, but it is probable that all such are due to traces of hydrocyanic acid that have not been removed. The seeds of many fruits contain amygdalin, some with and some without emulsin. If the ferment is not present, as is the case in sweet almonds, there is no possibility of the poison being set free. The water of bitter almonds, much used as a flavor and vehicle, often contains as much as 0.1 per cent. of hydrocyanic acid. Some liqueurs, as kirschwasser, maraschino, and persiko, contain small amounts of this poison along with other harmful substances.

The hydrocyanic acid nucleus is found in certain constituents of the animal body, and adenin, one of the purin bodies, seems to be a polymer of this substance. When adenin is injected subcutaneously in animals it has quite marked poisonous effects, and it is possible that it may be one of the autogenous poisons, about which much is said, but little known.

Action.—When a fatal dose of hydrocyanic acid is swallowed the duration of life is measured as a rule in minutes. The statement is often made that it kills instantly, but this term is relative and possibly an exaggeration; but it is nevertheless true that there is no poison more prompt in its action than this. On account of the deterioration of the officinal preparation hydrocyanic acid has acquired the reputation of being uncertain in its effects, but when the preparation is of proper strength its effects

are prompt in time and decisive in result. Wormly has collected a number of instances of poisoning with hydrocyanic acid. In the case reported by Hall (26) a suicide took one hundred drops of the pharmacopeial preparation. Hall found him within five minutes lying in a state of complete relaxation on the floor; his eyes were fixed, the pupils being normal, the pulse was 50, and becoming slower and feebler each minute; the respiration gradually became slower, with, toward the last, intervals of one minute, and death occurred within twenty minutes after taking the poison. In a case reported by Sewall (66) a man took seven drachms of Scheele's acid, the equivalent of twenty-one grains of the poison, then unlocked his door, called for help, stretched himself on his sofa, and was found dying, with stertorous breathing, in a few minutes. In the case reported by Hickman (28) a man swallowed by mistake an ounce and one half of the dilute acid, ran upstairs to call a doctor, returned to his pharmacy, and was given some ammonia and tincture of iron, but died within ten minutes after calling for help. In another of the cases collected by Wormly it is said that a French physician swallowed a teaspoonful of the medicinal acid, and fell dead as if struck by lightning. In a case reported by Arnold (2) a druggist had put chlorate of potash in a bottle containing hydrocyanic acid. The chlorate was prescribed for a child that died in convulsions immediately after swallowing the first teaspoonful of the solution. The attending physician then swallowed some, and barely escaped death, and the druggist, to prove that he had made no mistake, took the remainder of the prescription, and fell dead within a few minutes. The inhalation of the vapor that arises in decomposing a cyanid with mineral acid may cause speedy death. Such a case has been reported by Post (59). Within recent years the commercial uses of potassium cyanid have greatly multiplied, and accidental cases of poisoning have increased. The most extensive commercial use of the cyanid is the extraction of gold, and it is due to the discovery of this method of extracting the precious metal that the output of gold has become so great. Ores formerly regarded as worthless are now worked at profit. When the cyanid process was first employed the amount of the solvent used was much greater than subsequent experience has shown to be either necessary or desirable, and the danger of poisoning was greater. Auriferous ore is now extracted with a five-tenths solution of potassium cyanid which dissolves the gold. The solution is then passed over zinc shavings or some other finely divided metal, on which the gold is deposited. Nolan (52) reports a case of poisoning in a man who was employed in scrubbing the gold from zinc. Nolan's treatment of this case is of special interest. The hands and arms were immersed in very dilute sulphuric acid for several minutes at a time for several hours. Nolan states that the dilute sulphuric sets free hydrocyanic acid, which evaporates, while the heat facilitates the absorption and elimination of the sulphate of potassium which is formed. The vapor

formed by heating potassium cyanid is now used to some extent in disinfecting rooms. This, however, is a process which must be carried out with great care.

Silver and silver-plated articles are cleaned and brightened by immersing them in a solution of potassium cyanid, and then wiping them dry. Collins and Maitland (11) have reported a most interesting case of cyanid poisoning, with the clinical picture of poliomyelitis. The patient, an Italian of 38 years, was employed in cleaning the silver in a hotel. The strength of the solution used could not be ascertained, but the man stated that his hands and forearms were in the solution much of the time; that the skin became brownish and itched distressingly; that his nails became quite black, and that when he brought his hand near his mouth or nose he grew dizzy. Finally he was seized with severe diarrhea, his stools containing much mucus but no blood. Then he was mildly delirious for a few days; both ankles became stiff and there was severe pain in the legs. Both legs and arms grew weak, and he was unable to walk; there was retention of urine, and catheterization had to be employed. Eight weeks later the man was found bed-ridden, and unable to move the lower extremities, and the upper only slightly. Muscular atrophy was the most conspicuous objective symptom. For more than six months there was no indication of improvement, but slowly and imperfectly function returned, and the muscles began to fill out. The authors state the important features of this case as follows: (1) "The rapidity with which the symptoms came on and their intensity. In character they were of an overwhelming intoxication or infection; (2) the occurrence of spinal cord symptoms; (3) distribution of the atrophy and partial recovery."

The prompt and deadly action of hydrocyanic acid has led to repeated studies. Claude Bernard called attention to the fact that in animals poisoned with this agent the venous blood has the bright color of arterial, suggesting that the oxygen is not given off to the tissues. Since a like phenomenon is seen in carbon monoxid poisoning, and has been found to be due to the formation of a compound with this gas and hemoglobin, Hoppe-Seyler suggested that there might be a cyanhemoglobin compound, and proceeded to prepare such a body by the addition of hydrocyanic acid to blood *in vitro*. This apparently settled the question, but Hiller and Webber demonstrated that there is no cyanhemoglobin compound formed in the bodies of animals poisoned with hydrocyanic acid. In this way the observation of Bernard was left without satisfactory explanation until the classical research of Geppert (22). In the first place, Geppert made a careful study of the symptoms. In doing this he used a 1 per cent. solution of hydrocyanic acid, or its equivalent of 2.5 per cent. of potassium cyanid. From 0.1 to 0.2 c. c. of this solution injected into the jugular vein of a rabbit of 1,500 g. causes marked dyspnea; 0.3 c. c. leads to marked tremor, and 0.4 c. c. is followed by severe convulsions and arrest

of respiration. In order to study the symptoms satisfactorily Geppert found it necessary to give small doses subcutaneously, usually 1 c. c. per kilo of animal. Sometimes this was given in a single dose, and in other instances in broken doses. The first noticeable effect is an increase in the depth and volume of respiration; the intake may become two or three times the normal; then there are in dogs and cats vomiting and defecation; the movements of the animal become uncertain; it walks in a curve and one leg gets in the way of another; the dyspnea becomes more marked; the animal becomes less restless; it lies on the belly or sits; saliva pours from the mouth; up to this time the reflexes are undisturbed; the dog responds at least by look to call. This condition may continue for fifteen minutes, though seldom so long; then there are signs of the approaching nervous storm. The muscles of the face begin to twitch; in rabbits the aural vessels become bright red; a tremor flits over the whole body; then the head is thrown back on the neck and the whole body is involved in the clonic convulsions that follow one another in increasing intensity. In the intervals the animal lies limp and exhausted on its side, and with extended extremities; one may lift a foot, and when let go it drops like something dead; there is no response to call; there is no sign of life save the deep inspirations that come after prolonged intervals; the temperature falls several degrees; in cases terminating in recovery the respirations occur after less prolonged intervals, and slowly, with frequent interruptions, voluntary movements are resumed. Geppert divides the symptoms into the following stages:

(1) The preconvulsive, in which there are dyspnea, vomiting, defecation, incoördination, and slight fall in temperature.

(2) The convulsive, in which convulsions follow one another with great dyspnea, and a continued and gradual fall in temperature.

(3) The paralytic, in which the general and respiratory muscles are markedly involved, the reflexes are wanting, and there is the most pronounced fall in temperature.

(4) Return to normal. The respirations grow gradually more frequent; the temperature at first continues to fall and then begins to rise, and voluntary movements are slowly established.

When the vapor of hydrocyanic acid is inhaled the first stage is not observed, and the animal is stricken with convulsions at once. When a large amount of the poison is injected directly into the blood both first and second stages are not seen, and paralysis is immediate. It is interesting to note that in slight poisoning a return to the normal may be complete in from ten to twenty minutes, and that repeated injections of the same doses may be made at short intervals without marked effect. Apparently some immunity is secured.

Geppert has shown that in poisoning with hydrocyanic acid the oxygen absorbed by the tissues from the blood and the carbonic acid given off from

the tissues to the blood are both decreased. All life processes appear to be arrested by this poison, and it has been inferred that it owes its deadly action to its effect upon enzymes, but this is a mere assumption and nothing more. It is probably true that hydrocyanic acid does destroy ferments—possibly all ferments—but its deadly effect is due to a deeper and more far reaching action. It arrests chemical processes, as was shown by Millon, who found that formic acid fails to reduce iodic acid in the presence of hydrocyanic. This is quite parallel with the effect of hydrocyanic acid on the animal. The tissue is represented by formic acid, the oxyhemoglobin by iodic acid, and in the presence of hydrocyanic there is no reaction between the tissue needing oxygen and that carrying an excess of this element. Hydrocyanic acid owes its poisonous effects to the capability that it has of arresting the action of the living molecule. It arrests metabolism and consequently it is a poison to all forms of life, both the lowest and the highest.

In a recent research on the influence of cyanid on metabolism Richards and Wallace (61) show that nitrogen elimination is increased in this form of poisoning, and that cell dyspnea of fairly great intensity does not prevent urea formation.

Diagnosis.—Since poisoning with hydrocyanic acid is in the great majority of instances either accidental or suicidal, there is no difficulty in diagnosis. Moreover, the odor is easily recognizable, and quite characteristic, though it may be modified and marked by that of alcohol. The symptoms are quite similar to those due to nitrobenzene, but with the latter the effects are manifested much later.

Fatal Dose.—The exact dose of hydrocyanic acid taken in any given case is seldom known. The aqueous solutions are uncertain on account of the volatility of the acid, and the cyanid of potash often contains much carbonate. According to Garstang (20), an adult died after taking one half dram of the 2 per cent. acid, which is equivalent to 0.6 grain. In another instance death resulted within twenty minutes from 0.9 grain. It is safe to say that one grain of the acid or its equivalent in the form of potassium cyanid may cause death, and that one half this amount might induce serious and possibly fatal effects. Recovery from large doses has been reported, but this is probably due to preparations that have lost their strength.

Fatal Period.—In case the acid is free death usually occurs within a few minutes, generally within half an hour. If life is prolonged more than an hour recovery is likely. With the cyanid the time may be equally short, or it may be much longer, possibly some hours. In the prolonged cases it is probable that much of the cyanid has been converted into the carbonate.

Treatment.—In fatal cases, as a rule, death is so prompt that there is no time for treatment. The stomach should be washed out, and it has

been recommended that hydrogen peroxid or potassium permanganate be added to the water, with the view of converting the acid into the oxamid, but no time should be lost in searching for these additions because their effects are not so prompt as that of the poison on the tissue. Cobaltous nitrate is an antidote, but in excess would prove poisonous. It is not likely to be at hand, and is a dangerous thing to use if it were. It is claimed that by the administration of a mixture of ferrous sulphate and magnesium oxid the cyanid may be changed into the much less poisonous ferrocyanid. In the paralytic stage artificial respiration may be tried, but much cannot be expected from this procedure because the venous blood already contains an excess of oxygen. Death in hydrocyanic acid poisoning is not due to the lack of oxygenation of the blood, but to the failure of the tissues to take oxygen from the blood. Lang (41) has found that subcutaneous injections of sodium thiosulphate are of value in experimental animals.

Post-mortem Findings.—On opening the body of one dead from this poison the odor of hydrocyanic acid is generally quite evident, provided the obduction be made soon after death. The odor is said to be most persistent in the cranial cavity, but in time it is marked by the odors of putrefaction. The odor of nitrobenzene is similar, and is more lasting, that of hydrocyanic acid rapidly disappearing on exposure to the air. The skin as a rule shows no changes, except that dependent parts, especially the nails, may be bright red. This coloration is supposed to be due to the formation of cyanmethemoglobin. The jaws are usually firmly set, and there is a froth in and about the mouth. The mucous membrane of the alimentary canal may be quite normal, though occasionally ecchymoses are observed. When potassium cyanid is used the appearances of the mucous membrane of the alimentary canal may be similar to those induced by strong alkali. This salt is alkaline and, besides, much of it may be changed into the carbonate. When the cyanid comes in contact with the acid of the stomach hydrocyanic acid is liberated. From the alkalinity of the preparation the mucous membrane may be swollen, brown, or brownish red.

Elimination.—In part, hydrocyanic acid is changed into sulphocyanid in the body, and is eliminated in the urine in this form. However, we are quite ignorant of the disposition of the greater part of this poison when taken into the animal body. *In vivo* it apparently does not combine with hemoglobin. The poisonous effects of hydrocyanic acid on unicellular organisms are worthy of careful study.

The Caustic Alkalies

Locally the caustic alkalies destroy tissue in much the same way as strong mineral acids. However, there is this difference, the eschar formed

by the acids is hard and dry, while that induced by the alkalies is soft and gelatinous. Scar formation and resulting contractions are similar after acids and alkalies. The penetration of the tissue is deep, and perforation of the walls of the alimentary canal may occur. Stricture of the esophagus is a frequent result of the local action of the caustic alkalies. The effect of the subcutaneous injection of strong alkalies is influenced to an important degree by the injured part remaining free from bacterial infection, or by its becoming infected. The writer saw an example of this a few years ago when a physician injected strong ammonia in different parts of the body in a case of morphin poisoning. The necrosis of the muscular tissues was extensive around the point of each injection, but the blood vessels remained intact. On the other hand, when infection happens, the blood vessels may be closed by thrombi, and the nutrition of the part is impaired. The local action of strong alkalies upon nerves results in degenerative changes, which are histologically similar to those due to section of the nerve.

The strong alkalies, also their normal carbonates, are freely soluble in water. All are highly poisonous, but are seldom administered with criminal intent, most of the cases of poisoning with these substances being the result of accident.

Caustic Potash and Soda

Symptoms.—Strong solutions of these substances have an acrid taste, and instantly destroy soft tissues with which they are brought in contact. When swallowed the mucous membrane of the mouth and pharynx becomes white and swollen, and shows dissolved or necrosed patches. The mucosa of the stomach is macerated and corroded, exposing the reddened subjacent tissue. Immediately after swallowing there is a sense of constriction in the fauces and burning in the stomach. Violent vomiting usually results immediately, and the vomited matter is frequently stained with blood. There may be marked tenderness over the abdomen, severe purging with bloody stools, marked prostration, and in some instances convulsions. The mouth and throat and the upper part of the larynx are so inflamed and swollen that breathing is difficult. The face expresses great anxiety, the pulse becomes rapid and scarcely perceptible, and the surface is bathed with cold perspiration. If death does not occur there may be, after a few days, sloughing of the pharynx, and frequently stricture of the esophagus results. In some instances death is due to obstruction of the air passages. Although the carbonates of both potash and soda have a local caustic action, poisoning is practically limited to the first mentioned compound. This is due to the more markedly depressant action of potash, especially on the vasomotor center and the heart.

Lesser (45) reports the following cases: A boy four years old died

fifteen hours after he had swallowed a considerable quantity of a 14 per cent. solution of caustic soda. Bloody vomiting resulted immediately. Section made about 48 hours after death showed partial corrosion of the mouth and pharynx, and total destruction of the mucous membrane of the upper half of the esophagus. There were edema of the glottis, acute catarrh of the bronchi, and a pneumonic condition of the lungs. The stomach showed hemorrhagic spots, and there was a mild intestinal catarrh. In the second case a child two and a half years old died twenty hours after swallowing a small quantity of caustic soda of unknown concentration. Vomiting immediately followed. Post-mortem examination showed practically the same condition as that mentioned in the former case. However, the content of the stomach in this instance was still acid.

Treatment.—Lemon juice or vinegar may be administered, but these do not repair injured tissue. The stomach tube should not be used in poisoning with caustic alkalies for fear of rupture of the walls of the stomach or injury to the esophagus.

Ammonia

Symptoms.—This poison may be inhaled in the form of gas, or it may be taken into the stomach dissolved in water or in alcohol. In gaseous form it causes inflammation of the mucous membrane of the nose, mouth, pharynx, larynx, and bronchi. The conjunctiva may also be much inflamed, and prolonged exposure may lead to ophthalmia. The inhalation of ammonia causes free salivation, and this may be accompanied by nausea and vomiting. In some instances a pseudodiphtheritic membrane forms in the larynx and causes great dyspnea. Lehmann found that animals compelled to breathe air containing from two to three parts per thousand of ammonia gas showed salivation, inflammation of the conjunctiva, dyspnea, and convulsions, terminating in death. On section he found edema of the glottis, hemorrhage, and when death was delayed purulent bronchitis. Microscopic examination showed some of the alveoli quite normal, others collapsed, and still others emphysematous. The lung tissue was infiltrated with numerous leukocytes, and in the hemorrhagic foci unchanged red corpuscles were seldom seen, but leukocytes were abundant, and surrounded by pale red masses, and swollen epithelial cells. In animals that died during the experiment the most common and prominent lesions consisted of hemorrhagic tracheitis and laryngitis. The tracheal epithelium was extensively destroyed, and the cells stripped of their cilia. In the case of one animal that had survived an exposure of four and one half hours to a 5.5 per thousand atmosphere, but which died during a second experiment, Lehmann found purulent fibrinous pleuritis and pericarditis. He attributes the pleuropericarditis to the action of bacteria which had found their way into the blood through lesions caused by the gas. When

caustic ammonia is swallowed it inflames, and in patches destroys the mucous membrane of the mouth and pharynx. Usually vomiting immediately sets in and the ejected matter is frequently bloody. Even when death is due to swallowing ammonia post-mortem examination frequently reveals an acute bronchial catarrh. Perforation of the stomach occasionally occurs, and hemorrhage into this organ is quite generally found.

VEGETABLE POISONS

Strychnin

Occurrence.—Strychnin is the most important alkaloid found in nux vomica, which is the seed of the plant Strychnos Nux Vomica. This plant is native to the East Indies; its seeds are round, somewhat flattened; about an inch in diameter, slightly concave on one side and convex on the other, and are covered with grayish or yellowish hairs. Nux vomica is but little used at present in medicine, being supplanted by the more elegant preparations of its alkaloids, strychnin and brucin. These alkaloids exist in the seeds, combined with lactic and igasuric acids, strychnin being in the proportion of from 0.5 to 1.5 per cent. The only preparation of nux vomica which is now largely used in medicine is the tincture. This is of variable strength, depending upon the alkaloidal content of the seeds from which it is prepared. Strychnin is sold in the form of the alkaloid, and also combined with certain acids, the sulphate being the preparation most largely employed. The alkaloid forms a white crystalline powder—the form of the crystals varying from prisms to octahedra. It is only slightly soluble in water, requiring something more than eight thousand parts of this solvent at ordinary temperature. It is more readily soluble in alcohol and alcoholic solutions; in fact, the degree of its solubility in alcoholic preparations is largely dependent upon the amount of alcohol present. It is only slightly soluble in ether, but readily so in chloroform. Strychnin and its salts are intensely bitter, this property being readily detectable when one part of the alkaloid is dissolved in seventy thousand parts of water. However, Haines has pointed out the very important fact that the bitterness of strychnin varies greatly with different people. He has met with at least four persons who were unable to recognize the bitterness of this substance, and when some of it was placed on the tongue they stated that it had a rough or musty taste. Haines suggests that the use of tobacco and the existence of catarrh are important factors influencing the readiness with which the bitter taste of strychnin is recognized by individuals. He suggests that this is a matter of importance, inasmuch as it might be claimed by the defense in cases of suspected strychnin poisoning that the deceased did not complain of the

bitterness of the preparation which he took. The same authority points out the fact that the bitterness of strychnin and its salts may be largely masked by the presence of other substances, such as tannic acid, licorice, and chocolate. Ignorance of the relative solubility of the alkaloid played an important part in a case in which the writer was once interested. A certain man, whose reputation was not good, insisted on sending for an irregular physician for his wife, who was complaining of some slight ailment. After the irresponsible physician had prescribed the wife suffered from symptoms the description of which left but little doubt that they were due to strychnin. She then, on her own responsibility, sent for a reputable physician. This man came and, suspecting that the husband was attempting to kill his wife by the administration of strychnin, gave her a dose of medicine from his case and prepared a glass of medicine, leaving instructions that under no circumstances was a dose of it to be administered until a certain hour. Before the time for taking the medicine from the glass had arrived the doctor returned, noticed a crystalline deposit in the bottom of the glass, sent the husband from the room on some excuse, transferred the contents of the glass to a bottle, and refilled the glass with water. The suspicious crystals were sent to the writer for examination, and proved to be the alkaloid strychnin. On returning the second time to the house the doctor found again a crystalline deposit in the glass. This was also found to consist of crystals of the alkaloid. By this time the examination had been made, the husband was placed under arrest, a package of strychnin was found in his possession, he was tried, convicted, and sent to prison for life, while his wife escaped the death which he had desired to inflict.

Poisonous Action.—The symptoms induced by nux vomica and its alkaloids, strychnin and brucin, are fairly constant and characteristic. The rapidity with which they appear depends upon the form in which the poisons are taken and the condition of the alimentary canal at the time. The salts of the alkaloids are the most soluble preparations, and therefore symptoms appear more quickly after taking these than after the administration of the alkaloids themselves. Moreover, when taken upon an empty stomach absorption takes place rapidly, and the symptoms appear correspondingly early. Generally there is a sensation of numbness beginning in the extremities and passing over the entire body and terminating in a feeling of constriction about the throat and chest, and the muscles of the extremities begin to twitch. These movements grow more and more marked; the limbs are extended and perfectly rigid. Finally the whole body is thrown into a violent tetanic convulsion in which every muscle seems to participate. However, the spasm apparently begins in the extremities, rapidly extends over the trunk, and finally involves the face and jaws. Every extensor muscle in the body seems to be tetanized to the utmost, and even the toes and fingers may be extended; the head is thrown

back, and in extreme cases the entire body may be bent like a bow until only the heels and the back of the head touch the bed. This paroxysm varies in duration from a few seconds to as many minutes, and then gradually subsides, after which there is a respite, which varies in duration, and this is followed by another convulsion. These gradually increase in frequency and intensity. The respiratory muscles become so rigid that breathing is difficult; the pulse becomes weak and irregular; the countenance takes on a ghastly expression. The eyes are staring, the pupils are dilated, and often there is frothing at the mouth. As a rule the intellect remains unclouded, and the victim apparently realizes the gravity of his situation, and horror is depicted in every expression. During the intermissions the body may become greatly relaxed, and the individual presents the appearance of one who has greatly overtaxed himself by muscular exertion. Cold perspiration bathes the body, and the sleep of exhaustion may give temporary rest. In severe cases two or three, or at most five or six, of these paroxysms are sufficient to induce death. There is probably no other poison which gives such characteristic, easily recognizable symptoms as those induced by this alkaloid. Occasionally there are nausea and vomiting, and a certain amount of relief may be obtained in this way. The symptoms may be more or less masked by the simultaneous action of some other poison, such as morphin.

Poisonous Doses.—A quarter of a grain of the sulphate of strychnin has been known to cause death, and many authorities place the minimum fatal dose at 1-6th of a grain. In one well known instance, where a physician took by mistake ½ of a grain of the sulphate, death occurred in 18 minutes. Cases are given in which violent convulsions and threatened death have resulted from the administration of only 1-12th of a grain. However, this would not be likely to occur except in case of a very delicate person. The young are often found to be highly susceptible to this poison, and the writer has known slight manifestations, such as muscular twitchings of the extremities, to follow the administration of 1-30th of a grain in a nervous boy 16 years of age. A certain degree of tolerance to this drug may be established, and by beginning with small quantities the dose may in some instances be increased to 1-12th or even 1-6th of a grain. However, there is no evidence that very large doses, as in the case of morphin or arsenic, would be tolerated under any circumstances. In some there is manifested some evidence of cumulative action. Medicinal doses administered continuously for a time bring on slight symptoms of poisoning. Hypodermically 1-12th of a grain may in an adult cause marked symptoms. It should be stated that the fatal dose of strychnin as given by some authors is much larger than that stated above, some placing it as high as 2, and even 3, grains.

Time.—As is true of all other poisons, the time elapsing between administration and the appearance of the first symptoms, and that between

the administration and death, is very variable. In the majority of instances, however, the action of strychnin is rapid, and death usually occurs within from two to four hours, and if the last mentioned period be survived the chance of recovery, under proper treatment, is good. However, cases have been reported in which death did not occur until the 18th hour. In some of these delayed cases it is more probable that the oncome of death has been retarded by the treatment which has been resorted to.

Diagnosis.—As has already been stated, the symptoms of poisoning with strychnin are quite characteristic, and usually there is but little difficulty, on the part of the medical man at least, in recognizing them. The only disease the symptoms of which could be confounded with those of strychnin poisoning is tetanus; but even in this disease the differences from strychnin poisoning are sufficiently well marked to leave no room for doubt. In the first place, in the majority of cases of tetanus there is a history of injury, and the disease has come on gradually and progressed through a number of days, the convulsions growing constantly more frequent and more severe. Moreover, in strychnin poisoning, with each paroxysm the muscles of the extremities are first involved, and the extension of the tetanic spasm can be clearly seen as it passes upward over the limbs, reaches and involves the trunk, and last of all affects the muscles of the face, while, on the other hand, in tetanus the spasm usually begins in the muscles of the trunk or in the neck, and the muscles of the jaw are involved at an early stage. In tetanus there is usually some elevation of temperature, but this may also occur in strychnin poisoning, especially when the temperature is taken while the body is rigid. In dogs poisoned with strychnin the temperature of the rigid body may reach 107° F. We know of no recorded instance in which a medical man has been left in uncertainty as to his diagnosis between these affections, after seeing a single spasm, and the chances of confounding the two become infinitesimal when we are made familiar with the history of the case.

Treatment.—If the poison has been taken by the mouth, and this is usually the case, the stomach tube should be used at once. Unfortunately attempts to use the tube will often cause spasm. When this is the case the individual should be immediately thoroughly narcotized with chloroform, and then the stomach should be thoroughly washed. Dilute solutions of tannic acid may be used in the last washings, in order to precipitate, or at least render less soluble, any traces of the poison that may be left in the stomach. However, chemical antidotes should not be relied upon to the extent of doing away with the use of the stomach tube. After the stomach has been thoroughly cleansed the individual should be kept for hours, if necessary, fairly well under the influence of either ether or chloroform, or these may be used alternately. There is of course danger in the prolonged administration of chloroform, but the anesthetic may be pushed with the first evidence of returning spasm, and relaxed as the

spasm passes off. Absolute quiet is desirable. No one should be allowed in the room whose presence is not absolutely necessary. There should be no noise, and every draft of air likely to strike the patient should be shut off. Absolute quiet conduces to recovery. The administration of oxygen during the paroxysms has been recommended, but there is no recorded evidence that it has proved of value. Some advise the administration of chloral by the rectum. However, as compared with chloroform inhalation, the action of chloral thus administered is too slow and too uncertain to be depended upon in a case of poisoning with strychnin. The attending physician must realize that his treatment must be prompt and energetic, but quietly administered, if it is to be effective. In a case recently treated in the Hospital of the University of Michigan by Dr. Hewlett the patient received by mistake, at 8.30 a. m., 15 grains of strychnin sulphate. About one half hour later he began to have convulsions, the stomach was immediately and thoroughly washed out, and the individual was placed under the influence of chloroform and ether for six hours. He ultimately recovered.

Post-mortem Appearances.—The most striking thing after death from strychnin is the early appearance of rigor mortis. Indeed, an individual may die in a paroxysm and the body remain in this condition after death. Sometimes this rigor does not pass off until putrefaction sets in, and Haines reports a case in which a body was intensely rigid five months after death. However, too much stress must not be placed upon the early appearance of rigor mortis after death from strychnin. In truth, the statements on this subject in some of our text-books have led to unjustifiable claims in trials for murder. In at least one case the defense held that death could not have been due to strychnin because the body when dressed one half hour after death was found to be quite limp. Experiments with animals have shown that when minimum fatal doses are employed rigor mortis does not come on more speedily than it does after death from other poisons or from violence. The brain and spinal cord are usually congested, and there may be effusions of blood or serum. The heart is generally empty, though occasionally it is found to be distended. There is no characteristic finding in the stomach or intestines.

Elimination.—It is generally stated that strychnin is rapidly eliminated by the kidneys, and that in cases of suspected poisoning its detection in this fluid may be undertaken with confidence in its identification if present. Furthermore, it is claimed that as a rule elimination proceeds with marked rapidity, and even when poisonous doses have been given, followed by recovery, elimination has been found to be complete within from 24 to 48 hours. It is proper at this point to call attention to the fact that there has been some diversity of statement concerning the elimination of strychnin by the kidney, and, in fact, concerning its elimination from the body by any avenue. Dragendorff and his pupils came to the

conclusion from experiments upon animals that strychnin is not rapidly eliminated from the body, but that it is held for a time in the liver. Horsley held that strychnin disappears in the body by forming a new compound with albumin. Harley taught that it is oxidized and Uslar claimed that at the moment when strychnin manifests its toxic action it undergoes destructive changes in the body. Cloetta came to the conclusion from experiments upon the lower animals that strychnin is not eliminated in the urine. However, more recent investigations, among which we may mention those of Kratter, have shown that elimination with the urine occurs in the majority of instances, in man at least, speedily. The last mentioned author states his conclusions as follows:

(1) Strychnin is eliminated in the urine unchanged, and this elimination begins within a few hours.

(2) Elimination is in the majority of instances at least complete after forty-eight hours. (73.)

BRUCIN

Occurrence.—It is unnecessary to enter into any long discussion concerning this alkaloid. In toxic power it is much more feeble than strychnin. It is but little used in medicine, and the writer has found only the following cases of poisoning by this substance: Caspar (5) reports three cases of fatal poisoning with arsenic and brucin. Three children ate of bread and minced meat which was supposed to have been mixed with rat poison. This mixture was found on analysis to contain neither phosphorus nor arsenic, but a test for brucin apparently showed the presence of this alkaloid. However, neither brucin nor arsenic was found in the stomachs of the children. The only evidence of the presence of brucin in the food taken by the children was the fact that the residue from the alcoholic extract when treated on a watch glass with nitric acid gave a distinct red color. After carefully reading the report of these cases the writer is inclined to the opinion that death was due to kreotoxismus. The only brucin-containing substance which would be likely to be used as a rat poison is powdered nux vomica, and why brucin should be present while strychnin was absent is not easy of explanation. Certainly the evidence that death in these cases was due to either brucin or arsenic is not conclusive.

Christison (8) states that a species of bark commonly called false angustura was introduced into Europe by mistake for true angustura. This bark proved to be from the Strychnos Nux Vomica, which, according to Christison, contains only a small proportion of strychnin and a relatively large amount of brucin, and he reports two cases of poisoning. The first case, copied from Hufeland, occurred at Berne, Switzerland. The second case is stated as follows: "Professor Marc, of Paris, was once

violently affected with this poison, which he took by mistake for the true angustura to cure ague. He took it in the form of infusion, and the dose was only three-quarters of a liqueur glass full, yet he was seized with nausea, pain in the stomach, a sense of fullness in the head, giddiness, ringing in the ears, an obscurity of vision followed by stiffness of the limbs, great pain on every attempt at motion, lockjaw, and impossibility of articulating. These symptoms continued two hours, and abated under the use of ether and laudanum." There is no positive evidence in either of these cases that the active agent was not strychnin rather than brucin. The probabilities are that both were present. Sozinskey (67) reports a case of non-fatal poisoning which was due to a prescription given by an irregular physician. The prescriber claimed that he had copied his formula from a German handbook on popular medicine, published in 1840, and in this book was found a prescription which provided for 12 grains of brucin and half a dram of conserve of roses, to be made into 24 pills, four of which were to be taken twice a day.

Atropin

Occurrence.—Atropin is the active principle of atropa belladonna, or deadly nightshade, and is found in every part of the plant, but more abundantly in the root, in which the percentage varies from 0.2 to 0.5.

Properties.—The alkaloid is a colorless crystalline body of bitter taste, sparingly soluble in water, but readily so in chloroform and ether. It combines with acids, forming salts, the most important of which are readily soluble in water. The sulphate is the preparation most largely employed in medicine.

Symptoms.—The symptoms induced by belladonna and its alkaloid are fairly constant and quite characteristic. There is at first dryness of the mouth and pharynx; swallowing becomes difficult, the pupils rapidly dilate, and simultaneously vision is impaired. There is a marked and rather characteristic delirium in which there are hallucinations of vision and hearing, which at first are likely to be of a pleasant character, but later the voice becomes indistinct or is lost altogether, and the delirium is likely to become of a low muttering form. The individual picks at the bedclothes, or reaches out with thumb and finger into the air, and apparently grasps some object which he brings near his eyes for examination and then discards. He wishes to arise from bed, and when permitted to do so it is found that he has a staggering gait; coördination of movement is lost, and semblance of intelligence apparently disappears. The victim, if permitted to do so, may crawl about the room on all fours, and is likely to strike against objects which evidently he does not see. With very large doses there may be complete prostration, the extremities grow cold, the body is bathed in perspiration, the pulse becomes rapid and weak, and

coma may come on, and very rarely severe convulsions appear. Secretion from the kidney is generally increased, and involuntary emissions of urine may occur. In many instances a scarlatinous rash appears on the surface of the body. Nausea and vomiting are occasionally seen, but are rare. The only other poisons with which atropin may be confounded from an observation of the symptoms are the closely allied substances, such as hyoscyamin and scopolamin.

Poisonous Doses.—In children three berries from the deadly nightshade may cause marked symptoms, and twice this number may cause death. Of the sulphate of atropin, from 1-12 to 1-15th of a grain administered by the stomach and 1-32d of a grain given hypodermically may cause death. The writer has seen severe but non-fatal poisoning from 2 grains of the extract of belladonna. However, there are many instances in which recovery from very large doses has been reported. It must be stated, however, that in most of these the preparation taken has consisted of some part of the plant or some extract of doubtful strength, and not of the pure alkaloid or its salts.

Time.—The readiness with which symptoms appear after administration is largely dependent upon the form in which the poison is taken. When the sulphate of atropin is administered symptoms may show themselves within 5 or 10 minutes. By the expiration of this time dryness of the mouth and throat are plainly recognized, and dilatation of the pupils begins. When extracts of belladonna are administered absorption is more tardy, and several hours may elapse before the first symptoms appear.

Treatment.—When parts of the plant have been swallowed or extracts of belladonna have been taken, and the patient is seen relatively early, thorough washing of the stomach is of the greatest importance. In fact, when the alkaloid or its salts have been swallowed, it is well to wash out the stomach. Dilute solutions of tannic acid may be used through the stomach tube, and may be of some service in rendering the alkaloid less soluble. However, as we have frequently had occasion to state in speaking of other alkaloidal poisons, no great reliance can be placed upon chemical antidotes. As a physiological antidote pilocarpin has been recommended. However, it should be used with care, and the physician should always recognize the fact that pilocarpin itself has a markedly depressant effect, especially upon the heart. Most authors recommend that the delirium of atropin poisoning be controlled by the hypodermic administration of morphin. Again, the writer is inclined to speak a word of caution on this subject. It is undoubtedly true that there is a certain degree of physiological antagonism between atropin and morphin, but the physician who attempts to completely stay the delirium of belladonna poisoning by the hypodermic administration of morphin is in danger of doing his patient more harm than good. The hypodermic administration of a grain of morphin has been recommended, but the writer admits that although he

has treated many cases of belladonna poisoning he has never had the courage, nor has he found it necessary, to recommend such heroic doses of morphin. In fact, he has never used morphin for this purpose at all. The symptoms must be carefully watched, the patient must be prevented from injuring himself while in delirium; his pulse, when it becomes rapid and weak, may be strengthened by the subcutaneous administration of brandy, or by a strong dose of strychnin. The body should be kept warm, and above all things the physician in attendance must keep his own head cool and not further endanger the life of his patient by the administration of heroic doses of any so-called antidote. As has already been stated, recovery after very large doses of this drug has frequently been observed. The symptoms are alarming and distressing to friends, but the physician must not permit himself, while he is being urged to do something, to do that which might further jeopardize the life of his patient, and he should bear in mind that many apparently hopeless cases of belladonna poisoning recover, the per cent., according to Falck, being 88.4.

Post-mortem Appearances.—The pupils remain dilated for some time after death. In other particulars the evidence concerning the post-mortem appearances in poisoning with atropin has not been uniform. In animals poisoned with this alkaloid there is generally found marked hyperemia of the brain, of the abdominal viscera, and of the mucous membrane of the stomach. According to Hertwig there is in animals poisoned with atropin a venous hyperemia, especially marked at the base of the brain, and the medulla oblongata often shows blood extravasations. Gross (23) made a post-mortem examination after death which resulted from three grains of atropin, put up by a druggist instead of asafetida. The autopsy, made 48 hours after death, showed the pupils widely dilated, the face livid, and the blood vessels of the membranes of the brain distended. Otto (54) found hyperemia of the pia mater and medulla oblongata, and ecchymoses in the pericardium. According to Husemann (30) there is nothing characteristic in the post-mortem findings after death from atropin. The last mentioned author is undoubtedly correct in his statement, because every condition which has been supposed to be at all characteristic after death from atropin may be found after death from other causes.

Kratter (40) found after poisoning with belladonna berries a dark violet coloration of the mucous membrane of the pharynx and a croupous inflammation of the lower third of the esophagus; the former was due to the color and the latter to the irritating effects of the berries. Paltauf (55) detected the coloring matter of the berries in the stools.

Gelsemin

Occurrence.—This is the active principle of gelsemium sempervirens, or yellow jasmin, and is found in the root of this plant in the proportion of

about 0.25 per cent. The alkaloid was obtained first by Wormley in 1870, who, at the same time, demonstrated that the plant contained a non-nitrogenous body to which the name gelsemic acid was given. There are really two alkaloids in yellow jasmin, one, gelsemin, discovered by Wormley in 1870, and another, gelseminin, isolated by Thompson in 1887. The plant also contains a non-nitrogenous body that forms fluorescing solutions, designated by Wormley as gelsemic acid, but subsequently found by Schmidt to be identical with an organic body found in many plants. The alkaloid is not used in medicine, and preparations from the plant are but seldom employed by regular physicians. For many years gelsemium was a favorite remedy with so-called eclectic physicians, and several deaths resulted from preparations used by practitioners of that school.

Properties.—The alkaloid is an odorless, colorless, bitter substance which crystallizes with difficulty and imperfectly. It is easily soluble in ether and chloroform, and only sparingly soluble in water. It has marked basic properties, and unites with acids, forming salts which are readily soluble in water.

Poisonous Action.—There is no known case of poisoning with the alkaloid itself. Poisonous doses of the various preparations of the plant induce, first, a sensation of muscular weariness and relaxation. The gait becomes unsteady on account of impaired coördination. The action of the heart is depressed, and the pulse becomes feeble and irregular in the majority of instances, although cases have been reported in which it was stated to be unusually strong. Sight is impaired, and the victim seems bewildered. In some instances there is double vision, and all objects take on a yellow tint. There may be total blindness, and instances of paralysis of the upper eyelids have been observed. At first the face may appear congested, but later it becomes deadly pale, and the lips are blue. The lower jaw droops, the tongue seems thick, and speech is imperfect, and the voice may be altogether lost. The respirations become slow, irregular, and stertorous. As a rule the mind remains clear until either coma or convulsions set in. Death is apparently due to failure of respiration.

Treatment.—The prompt and thorough use of the stomach tube should be the chief reliance in the first stages of poisoning with preparations of gelsemium. After the absorption of poisonous quantities artificial respiration and heart stimulation must be the main reliance; in securing the former electricity may be of service; for the latter hypodermic injections of strychnin and intravenous injections of the aromatic spirits of ammonia may be of service. The hypodermic administration of digitalin has been recommended by some, and of morphin and atropin by others, but both are doubtful procedures. The body should be kept warm by the application of external heat and the giving of hot drinks.

Veratrin

Occurrence.—There are a number of alkaloids found in both veratrum album, or white hellebore, and veratrum viride, or American hellebore. Fluid extracts and tinctures of veratrum viride have been used quite extensively.

Poisonous Action.—Physiologically veratrin and jervin, also the less important alkaloidal bodies found in the veratrums, have the same action. When swallowed there are a burning sensation in the mouth, constriction of the throat, intense heat in the stomach, nausea, vomiting, and purging. These symptoms of gastrointestinal irritation are followed by marked prostration, vertigo, dilatation of the pupils, impaired speech, feeble action of the heart, cold extremities, insensibility, and convulsions. Christison (6) reports the poisoning of a family of eight from the eating of bread in which the powdered root of veratrum album had been used instead of cumin seeds. All were seized with pains in the stomach and bowels, with a "sensation as if the whole intestines were wound up into a clew." While gastrointestinal irritation is apparently accountable for the most prominent symptoms, there are cases on record in which the effects on the nervous system seem to have predominated. In these instances severe convulsions have set in early, and usually have continued until death. Caspar reports the accidental poisoning of a family with veratrum. The mother died and the others recovered. The symptoms were nausea and vomiting. In the dead body Sonnenschein found veratrum.

Poisonous Dose.—It is impossible to make any definite statement concerning the poisonous dose of either veratrin or jervin, as there are no instances on record in which either of these alkaloids has been taken in fatal quantity. A half dram of the tincture of veratrum viride, and twenty grains of the powdered veratrum album have proved fatal. However, there are many instances in which recovery has followed very large doses. It seems probable that in these the preparations from the plant were not rich in alkaloidal content.

Treatment.—The thorough use of the stomach tube is recommended, with repeated washings with warm water. The depressing effect of the poison should be combated by the administration of stimulants, and the action of the heart may be strengthened by the subcutaneous injection of strychnin, or the intravenous injection of the aromatic spirits of ammonia. Some recommend that after the thorough evacuation of the stomach morphin should be administered in order to control the pain. The wisdom of this recommendation is questionable. A physician should always be slow in the administration of morphin in the treatment of any case of poisoning in which prostration is imminent.

Post-mortem Appearances.—Usually after poisoning with any of the preparations of veratrum there is found a congested state of the stomach

and intestines. The lungs and brain are often filled with blood, and this condition is in many instances at least due to the vomiting, and is by no means characteristic of the action of this poison.

Digitalin

Occurrence.—The poisonous properties of digitalis purpurea, or foxglove, are due to a number of active principles, the most important of which are digitalin and digitoxin. These are glucosids and not alkaloids. Digitalin does not contain nitrogen, and when boiled with dilute mineral acid glucose is one of its decomposition products. Both digitalin and digitoxin form colorless crystals of acrid or bitter taste. They are with difficulty soluble in water and in ether, but readily soluble in alcohol and chloroform. Commercial digitalis varies widely in composition, but both its poisonous and therapeutic properties are due to the glucosids which it contains.

Poisonous Action.—When poisonous doses of digitalis are swallowed there is a marked gastrointestinal irritation. Severe pain in the stomach soon manifests itself, extends to the bowels, and is accompanied by severe vomiting or purging, or both. The action of the heart becomes irregular, and the number of pulse beats may be reduced to one half the normal. The extremities become cold, the surface is bathed with moisture, the pupils are dilated, vision is imperfect, the intellect is at first bewildered, and then delirium comes on. Finally convulsions, generally followed by coma, lead to death.

The readiness with which symptoms appear after swallowing preparations of digitalis varies greatly, depending upon the form in which the drug is administered and the condition of the individual at the time. The action of digitalis after its absorption begins is, compared with many other poisonous vegetables, somewhat slow. Even when large quantities are taken death seldom occurs within twenty-four hours, and may be delayed for several days. Indeed, one case is reported in which death did not occur until after the lapse of three weeks, during all of which time the heart remained under the influence of the disturbing action of the poison.

Poisonous Dose.—It is impossible to say what the minimum fatal dose to man of either of the glucosids is. The preparations of digitalis most frequently used are the tincture and the infusion. These vary quite markedly in strength. Then, again, digitalis belongs to the list of cumulative poisons, and in nearly all instances where harm has resulted from its medicinal employment the injurious effect cannot be ascribed to any single dose, but is the result of the long-continued administration of the drug. Death has been known to follow 36 grains of the powdered leaves and one dram of the tincture. Two milligrams of digitoxin caused serious effects, and it is probable that twice this amount would kill. Children

have been severely poisoned with minute doses of Nativelle's digitalis, but there are preparations of "digitalin" the usual doses of which are from 6 to 30 milligrams.

Treatment.—The thorough use of the stomach tube in the early stages is the only efficient remedy. If this be not at hand vomiting, if already present, should be encouraged by the administration of such mild remedies as mustard and warm water; and if not present should be developed by the same agents. Rest in a recumbent position is an essential for some time, even after the acute symptoms have passed away. Attempts to take the standing position may induce heart failure and death. When the extremities are cold hot applications should be made, and heart stimulants administered.

Colchicin

Occurrence.—Colchicin is the active principle of colchicum autumnale, or meadow saffron, in which it exists to the extent of from 1 to 2 per cent. Preparations of this plant are used medicinally, but the alkaloid is not employed except in scientific investigations.

Properties.—Colchicin crystallizes with difficulty, and usually appears as a white amorphous powder, readily soluble in water, alcohol, chloroform, and ether. Its aqueous solutions are bitter and acrid. Its basic properties are not marked, and it combines with acids tardily.

Poisonous Action.—Colchicum and its alkaloid are gastrointestinal irritants, and symptoms are confined almost wholly to the alimentary canal. It is quite as irritating as any of the non-caustic mineral poisons. When swallowed in excessive quantity it induces intense burning pain in the stomach and bowels, followed by nausea, vomiting, purging, and tenesmus. Then there result marked prostration, coldness of the extremities, feeble action of the heart, irregular respiration, and death. In the majority of fatal instances death seems due to exhaustion, and seldom occurs in adults within 24 hours, and it may be delayed several days. It is impossible to make any positive statement concerning the fatal dose of the alkaloid, except by inference from the effects of other preparations. In this way we learn that from one-third to one-fourth of a grain might prove fatal to an adult. Fatal results have followed the administration of three drams or more of the wine of colchicum. It is not strange that in case of a poison which acts so powerfully as a gastrointestinal irritant that recovery should sometimes follow the administration of very large doses. These undoubtedly are due to the early onset of vomiting and purging, by means of which a large portion of the ingested material is cast out of the body before it has time to manifest its poisonous properties. Wachholz places the fatal dose of colchicin at 0.06 gram, and states that he has known of three deaths from it when given for osteomalacia. A popular remedy for gout, used in Germany, has also been responsible for one or more deaths.

Coniin

Occurrence.—Coniin is the active principle of the highly poisonous plant hemlock, the action of which has apparently been known to man from the most remote historical times. The alkaloid is found in every part of the plant, existing in combination with an organic acid, but it is found most abundantly in the fruit, in which it is present to the extent of from 1 to 2 per cent. Conium maculatum is one of the most widely distributed of the umbelliferous plants. It is frequently mistaken for parsley, sometimes for asparagus, and cases of accidental poisoning are by no means infrequent. It is believed to be the poison which was used by the ancient Greeks for the purpose of legal execution. The per cent. of alkaloid in the plant apparently varies with the season of the year. However, the extent to which this variation occurs is a matter which needs more exact investigation, inasmuch as the amount of coniin found is so largely dependent upon the conditions and methods attending its extraction.

Properties.—Coniin belongs to the volatile alkaloids, and at ordinary temperature is an oily fluid, slightly lighter than water and of unpleasant odor, said to resemble the urine of mice. It boils at 163.5° C., and is only slightly volatile at ordinary temperatures. The free alkaloid is soluble in about 100 parts of water, and freely soluble in chloroform, alcohol, and ether. It is decidedly alkaline in reaction, and readily forms salts, most of which are solids at ordinary temperatures. Aqueous solutions of the alkaloid give precipitates with tannic acid, silver nitrate, and other general alkaloidal agents. When left in contact with the air a slow process of oxidation occurs, and the alkaloid finally becomes converted into a brownish resinous body.

Poisonous Action.—The general effect of coniin upon the animal body is to cause paralysis of the muscular system. This generally begins in the voluntary muscles and gradually extends over the trunk, involving the muscles of respiration, including the diaphragm, and leading to death from asphyxia. In some instances muscular twitchings and transient convulsive movements interrupt the progress of the paralysis. The muscles of the heart apparently escape the action of the poison, and it may be seen to beat in experimental animals some time after respiration has ceased. At first there is marked muscular weakness, accompanied by difficulty in walking, and later by inability to maintain the erect posture. The voice becomes feeble and may be lost altogether. There is dilatation of the pupils and, in the later stages, loss of vision. The intellect remains clear until respiration becomes so impaired that the blood is overcharged with carbonic acid gas. Delirium and unconsciousness, passing into coma, may precede death. The action of the alkaloid, as well as that of active preparations from the plant, is prompt. Symptoms generally appear within a few minutes after the poison has been swallowed, and death may occur

within one hour, although, when preparations of the plant are eaten, from three to four hours usually supervene. Upon the rapidity of its action Christison (7) makes the following statement: "A single drop applied to the eye of a rabbit will kill it in nine minutes, and three drops in the same way will kill a strong cat in a minute and a half. Five drops introduced into the throat of a little dog began to act in 30 seconds and proved fatal in one minute; and when 2 grains neutralized with 30 drops of weak hydrochloric acid were injected into the femoral vein of a young dog it died before there was time to note the interval, so that only two or three seconds at most had elapsed before all the internal signs of life were extinct. This extraordinary rapidity of action seems incompatible with its operation taking place by conveyance of the poison with the blood to the spinal cord."

It is generally stated that one drop of the alkaloid is sufficient to cause death. While this is probably true, the evidence upon which it is made is unsatisfactory so far as the statement applies to man. We know of no instance in which so small a quantity of the alkaloid has proved fatal to man. Indeed, cases of poisoning have usually resulted from the taking of some preparation of the plant, and the amount of the alkaloid present in the doses swallowed is an unknown quantity. However, if it be as poisonous to man as it is to the lower animals, it is safe to say that one drop of the alkaloid would be likely to produce a fatal result.

Treatment.—The stomach should be thoroughly washed in all cases. This, however, would be of but little service provided the alkaloid or any of its salts in pure form had been swallowed, so great is the rapidity with which absorption takes place. In case of poisoning with preparations of the plant one may hope to remove a portion of the substance by washing out the stomach. The use of chemical antidotes is of no value, and time should not be given to their consideration. Stimulants, such as alcohol, and the aromatic spirits of ammonia, also strychnin, should be promptly employed. Artificial respiration may be resorted to, and may be aided by the proper application of electricity. The inhalation of oxygen theoretically is of value, but it cannot be of much service unless artificial respiration is carried on simultaneously.

The water hemlock, or cicuta verosa, contains a poison, the exact nature of which has not yet been determined, but the symptoms induced by it show that it is not coniin. A few years ago the writer saw three children who had been poisoned by this plant. Within from two to four hours after they had eaten it they were seized with most violent tetanic convulsions, accompanied by marked opisthotonos, and this continued at intervals, varying from a few minutes to half an hour, and grew in intensity, and all of the children died within twelve hours after they had eaten of the plant. This accident happened in April. It is believed that at certain times of the year the cicuta contains no poison.

The plant known as hemlock, dropwort, or dead tongue and œnanthe crotata, seems to be poisonous in certain climates, and wholly free from poisonous properties when grown in other places. In regard to this plant Christison (9) makes the following statement: "Since Lobel first took notice of the poisonous properties of the œnanthe root in 1570 an uninterrupted series of observations has been published down to the present day, showing that in France, Germany, Holland, Spain, and various parts of England, as far north as Liverpool, it is at all seasons of the year, even in October and the beginning of January, a poison of great activity. In several of the cases death has been occasioned by a single handful of the roots, in one instance by a piece no bigger than the finger, or in other cases by individuals merely tasting them. A girl seems to have had a narrow escape after merely eating, after the interval of three hours, two pieces of the size of a walnut. Very seldom has death been delayed more than four hours, and on some occasions a single hour has been sufficient. Sometimes the symptoms have been slow in making their appearance, an hour and a half having occasionally elapsed before the effects were evident; but in every instance their progress was rapid, once the symptoms had fairly set in, and some died in convulsions almost immediately after being taken ill."

Fools' Parsley, or æthusa cymapium, is another poisonous umbelliferous plant. It causes nausea, vomiting, pain in the stomach, and numbness of the limbs, followed by coma which may terminate in death.

Nicotin

Occurrence.—Nicotin is the active principle of tobacco, or nicotiana tabacum. Combined with an organic acid the alkaloid is present in every part of the plant, the amount varying in different varieties from two to ten per cent. There is no other plant which contains this alkaloid. Although pure nicotin is a most deadly poison the plant containing it is used in a great variety of ways, and by some in very large quantity. From this we must conclude that as it exists in the plant nicotin is not readily absorbed into the body. However, there are many cases of poisoning from the plant on record, but it must be admitted, after we have taken all the possibilities into consideration, that a certain degree of immunity to this poison is acquired by those who use the weed. The effects of the first smoke or chew need not be described. They are familiar to most males who have reached years of maturity. Gmellin reported two cases of death from excessive smoking, one man having smoked seventeen and the other eighteen pipes at one sitting. Lanzoni reports a death which resulted from taking too much snuff. Cases of poisoning from the application of the leaves of tobacco locally for the relief of ringworm have been reported, and in some of these the termination was fatal. Infusions of tobacco were

once used by rectal injection in the treatment of constipation by irregular practitioners, and death from this cause has been reported. Rectal injections were also used at one time for the purpose of destroying pin worms, and in some of these cases death was caused. Insane people have swallowed large quantities of the leaf and of infusions of tobacco, and in some of these death has followed. It is stated that one of the lesser French poets of the past century was killed by drinking a glass of wine into which a box full of Spanish snuff had been emptied by a half drunken companion.

Properties.—Pure nicotin is a colorless liquid which has the characteristic odor of tobacco. It is freely soluble in water, alcohol, ether, and chloroform. It is alkaline in reaction, and combines with acids, forming neutral salts. On exposure to the air it is slowly oxidized, and is gradually converted into a brownish resin. It is slowly volatile at ordinary temperature, but does not boil until it is heated to 250° C.

Poisonous Properties.—Nicotin is the only active agent in tobacco, and therefore all the poisonous symptoms which result from the administration of preparations of this plant are due to this poison. When taken in excessive quantity it causes nausea and vomiting, giddiness, trembling of the limbs, marked prostration, accompanied by muscular weakness, feeble action of the heart, slow respiration, and dilatation of the pupils; although the action on the pupils is by no means constant, and they are sometimes found to be contracted. In extreme cases the limbs become cold, the body is bathed with perspiration, the face is blanched, and intellect is impaired.

When pure nicotin is administered, as it was in a celebrated case in France, death may occur within a few minutes, and the records of the earlier part of the 19th century show numerous instances in which death occurred within half an hour or less time after the employment of rectal injections of infusions of tobacco. Much experimental work has been done on the effect of nicotin on the lower animals, and of especial interest is that part of these researches in which the causal relationship between this poison and arteriosclerosis has been investigated. Josue (33) practiced intravenous injections of nicotin, but without result, as his doses were very small, and possibly his preparations were not good. Adler and Hensch (1) found that 1.5 mg. of this alkaloid injected into the ear vein of a rabbit causes in about ten seconds a violent convulsion that lasts from three to five minutes, after which the animal rapidly recovers. When the injection is repeated daily there is no immunity nor tolerance, and necrotic lesions are produced in the aorta. Collins (10) states that he and Brooks have induced arteriosclerosis in rabbits by causing them to inhale tobacco smoke.

Poisonous Dose.—It is impossible to say just what the smallest fatal dose for man is. It is probably, however, only a fraction of a grain. In-

fusions of the plant vary widely in toxicity on account of corresponding variations in alkaloidal content.

Treatment.—The stomach tube should be thoroughly used, provided the poison has been administered by the mouth. In case rectal injections have been employed the colon should be freely irrigated. Stimulants, such as alcohol, aromatic spirits of ammonia, and strychnin, may be administered. When there is evidence of failure of respiration artificial means should be resorted to for the purpose of maintaining this function, and in doing this electricity may be of service, but I know of no cases in which it has been employed.

Cocain

Occurrence.—Cocain is the active principle of a South American plant known as erythroxylon coca. It is found most abundantly in the leaves, where it exists, together with two relatively unimportant alkaloidal substances, combined with an organic acid. The fresh leaves yield from 0.2 to 1.2 per cent. of the alkaloid. As the leaves dry and decay they become inert on account of the gradual decomposition of the alkaloid.

Properties.—The alkaloid cocain is a colorless crystalline body, readily soluble in alcohol, ether, and chloroform, sparingly soluble in water. It is alkaline in reaction, and combines with acids, forming neutral salts which are readily soluble in water. The hydrochlorid is the preparation most generally employed in medicine, and is the form in which the drug is most extensively used.

Poisonous Action.—Salts of cocain are rapidly absorbed, and are poisonous when applied to any of the mucous membranes of the body. Acute cocain poisoning is rare, but chronic poisoning, due to the establishment of a habit, unfortunately has within the last few years become quite common. In acute cases there is a sensation of fulness in the head. This is usually accompanied by nausea and vomiting, although symptoms on the part of the stomach may be wholly wanting. At first the pulse is increased in frequency, but later the number of beats falls below the normal. Respiration becomes shallow, slow, and labored. As the effects progress the extremities become cold, the body is bathed with perspiration, the pupils are dilated, the surface of the body shows by its cyanotic condition lack of oxidation of the blood. The pulse grows more and more feeble, and finally becomes imperceptible. At the same time the respiration becomes more labored and, as the blood fills up with carbonic acid gas and other poisonous substances, the brain becomes clouded, delirium, sometimes of a wild kind, sets in, convulsions may occur, the individual falls into a comatose condition, and death results. The writer once saw most alarming symptoms result from the injection of 1 c. c. of a 4 per cent. solution into the gum preparatory to lancing an abscess.

In chronic poisoning with cocain the victim becomes a nervous wreck. His gait is somewhat uncertain on account of incomplete coördination. As the effect of the drug passes off he suffers from a sensation of lassitude, and feels the need of a stimulant. The continued use of the poison dims the mind. Hallucinations while under its influence are subsequently mistaken for facts, and the cocain habitué becomes a moral and physical degenerate. Some of the most widely used catarrh and asthma cures contain cocain. The victim is relieved from the most annoying symptoms of the disease, but becomes a slave to the drug, and finally a broken-down, nervous wreck.

When the hydrochlorid is administered hypodermically, given by the mouth, or injected into some cavity, such as the bladder, absorption may take place very rapidly, and if the dose be sufficiently large death may occur in a few minutes. In fact, when administered subcutaneously, death may occur in a few minutes.

Treatment.—If the poison has been administered by the mouth the stomach should be washed out. Indeed, this is a wise procedure in case of poisoning with any alkaloid, irrespective of the avenue by which it has been administered, because, even when given subcutaneously, most of the vegetable alkaloids are in part at least eliminated by the mucous membrane of the alimentary canal, and a certain portion thus reaches the interior of the stomach, from which it would be reabsorbed if it were not washed out. It is well to bear this in mind, not only in the treatment of cocain poisoning, but in dealing with poisoning with other vegetable alkaloids, and to remember that thorough lavage of the stomach should not be omitted, whatever the method of administration may have been. The depressing effects of the poison are to be antagonized by artificial respiration, flagellations with cold cloths, and the hypodermic or intravenous injections of heart stimulants, such as the aromatic spirits of ammonia and the sulphate of strychnin. In chronic poisoning gradual withdrawal of the drug may lead to relief from the habit. However, like other similar bad habits, the individual when left to himself often has not the moral strength necessary to enable him to resist temptation. For this reason confinement in some special institution where a certain degree of restraint can be practiced is highly desirable.

Aconitin

Occurrence.—Aconitin is the active principle of aconitum napellus, which is sometimes known as wolfsbane, and at other times designated as monkshood. The alkaloid, combined with an organic acid, is found in every part of the plant, but is most abundant in the root, where it exists in proportions varying from 0.1 to 0.8 per cent. There are less important alkaloids in the same plant, and there are other varieties of aconitum in

which there are alkaloids differing but slightly from aconitin. The alkaloid is but seldom seen, and the medicinal preparation most extensively used is the tincture.

Properties.—The alkaloid is a colorless crystalline body which combines with acids, forming salts. The alkaloid itself is only sparingly soluble in water, readily soluble in chloroform, less so in ether. Its salts are easily soluble in both alcohol and water. The aconitin purchased in the market varies greatly in its purity, and some samples contain only traces of the alkaloid. Indeed, some years ago Wormley showed that certain specimens of so-called aconitin exported from Germany contained absolutely no trace of the alkaloid.

Poisonous Action.—Poisoning with aconite is generally accidental, and for the most part has been due to the administration of some preparation of the plant, or to mistaking the plant for celery or some other vegetable. According to Stich (69) there are only two cases of the homicidal employment of aconite on record. When a poisonous dose is swallowed the first symptom observed is a peculiar numbness which usually begins in the lips and tongue, then gradually extends to the pharynx. This numbness is peculiar, inasmuch as it is accompanied by a tingling sensation. Later there may be more or less pain in the stomach. However, as a rule this is not marked. Soon the effects due to the systemic action of the poison begin to manifest themselves. The peculiar numbness which first appeared in the lips or tongue now manifests itself in the fingers and toes, and it gradually extends up the extremities and finally involves the trunk. There is more or less loss of sensation accompanying this numbness, and, while there may be marked lassitude and disinclination to muscular movement, there is at least at this stage no paralysis of motion. As the numbness of the extremities accompanied by the peculiar tingling becomes more marked and more extensive the surface of the body becomes cool; the face is pale, there is free flow of perspiration, the action of the heart becomes feeble, the pulse is reduced to a thread, and finally becomes altogether imperceptible. There may be at this stage more or less well-marked tetanic convulsions, but as a rule these are of short duration. The individual passes into coma, the action of the heart grows more and more feeble, and death results from failure of this organ.

Fatal Period.—In large doses aconite may speedily cause death. Indeed, when death is due to the primary action of the drug it occurs within a few hours, but there are cases which linger along for a few days and in which the heart is not able to recover its normal tone, and death may occur four or five days, or even longer, after the poison has been swallowed. Mallet reported on six cases of aconite poisoning that occurred in an insane asylum in Virginia, the shortest period being eight minutes, and the longest four days.

Poisonous Dose.—It is impossible to state just how much pure aconitin

constitutes the minimum fatal dose for man. This has been estimated variously at from 1-50th to 1-16th of a grain. It is possible that these estimates may be fairly correct, but the evidence upon which they are based is not reliable. In the first place, as has already been stated, preparations of the so-called alkaloid vary greatly in strength, and some of them are wholly inert. In the second place, the number of cases of homicide on record is exceedingly small, and in cases of accidental poisoning preparations of the plant have always constituted the material taken. Four or five drops of the tincture may produce numbness of the lips and tongue, and even of the extremities, and one dram may cause death. Indeed, at least one case is upon record in which twenty-five drops of the tincture proved fatal.

Treatment.—The stomach tube should be used promptly; then heart stimulants, such as ammonia and strychnin, may be employed. If at hand, tannic acid may be dissolved in the water used in washing the stomach, but the washing should not be delayed in order to obtain tannic acid.

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